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3RD INTERNATIONAL MEDICAL CONFERENCE "INFERTILITY 35+" SUPPORTING COMPANIES

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Georgian-German Reproductive Center (GGRC) is organizing the 3rd International Scientific Conference “Infertility 35+” in Tbilisi at Biltmore Tbilisi Hotel as well as on line on Zoom platform on September 18 -19 2022.

The participants of the conference will have the opportunity to listen to the presidents of reproductive associations of different countries and doctors of the world’s leading clinics from USA, Canada, Austria, Latvia, Estonia, Israel, Germany, Turkey, Kazakhstan, Ukraine, France, Russia, Armenia, Azerbaijan.

- “News in assisted reproductive technologies and methods”;
- “Importance of genetic studies in reproductive medicine”;
- “Pregnancy management during diabetes”;
- “Receiving biological material of oncology patents”;
- “Rising Infertility Statstcs and Studies”;
- “Isolaton of stem cells and PRP procedure” etc.

The participants of the conference will get to know the details of the workshop which will be held in the small operating block and embryology laboratory of GGRC.- Topic "Isolation of stem cells and PRP procedure" – GGRC laboratory is the only one that has FDI and ISO certificates.

The conference is supported by the Ministry of Labor, Health and Social Protection of Georgia.

According to the decision of the N14 session of the Professional Development Council on June 24, 2022, the conference format program – "Infertility 35+" (Acr. N C0359) was awarded 1 type 9 UPG points for "Reproductive Medicine", "Obstetrics and Gynecology", "Urology", "Clinical Oncology" , for doctors certified in "endocrinology" and "oncosurgery".

The registered participants of the conference will be given appropriate certificates.

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ARTIFICIAL ABORTION – THE GEORGIAN STORY

Abstract

The chapter includes the short description of the current situation of artificial abortion and contraception in Georgia with the stress of its specific features. Second part of the material is devoted to the principles of elimination of restrictive policy on artificial abortion and contraception. And the final and main topic of the material represents the author's thoughts and philosophy of abortion and life issues.

Keywords: Artificial abortion, Contraception, Reproductive health.

The reader may wonder: Why the Georgian Story?

1. Maybe, because Georgia is the first and the only country in the world, where Reproductology, the science about both, woman's and man's reproductive health, has widely been recognized as the officially independent medical discipline, starting from 1997, not just the part of obstetrics and gynecology;
2. Georgia possesses a nonofficial record in the fast-spreading of modern contraception. In any case, according to the research of the Zhordania Institute of Reproductology (the oldest clinic of this type in the world, established in 1958) in Georgia, in 1987, when the population averaged 5.5 million, the artificial abortion total rate was 300 000, two-thirds of which was illegal, approximately 2-4 abortion per woman. In this period, Georgia was a part of the Soviet Union, which was the first in the world abortion statistcs, and Georgia

was one of the leaders among the Soviet republics. Furthermore, the usage of modern contraception was 0 (zero), which means that contraception, as the regulatory method of reproductive function, did not exist in our country.

By the year of 2010, the prevalence of modern contraception exceeded 70%. We consider this jump from 0 to 70 percent as a unique fact, and we rely on the Zhordania Institute's studies, but not the CDC's data, which we consider not reliable since the study was carried out with the serious omissions: men were not included in the research;

3. We are very proud that our country is the one in the Christian world, where the absolute understanding has been reached between the Church and the reproductologists. For example, my colleagues and I never had real problems in the development and use of In Vitro Fertilization (IVF). In our opinion, all the above-mentioned is the result of permanent and frequent consultations between the Georgian Orthodox Church and the Zhordania Institute of Reproductology. We think that our experience will benefit the Christian countries, which have problems in developing and using the main principles of reproductive health.

Concerning the contemporary dynamics of abortion and contraception, our experience points out, that the abortion rate is 10 thousand, and the use of contraception reaches up to 90%. It may be said, that the unpleasant phenomenon of abortion is defeated in Georgia. The same is shown in the statistical analysis of the latest years (Unfortunately, only up until 2010. After this then, no research has been conducted due to unstable political situation and inattention of the Government) and in the results of interested specialists' permanent surveillance in the Zhordania Institute. To be more exact, artificial abortion is not eliminated totally. Disappointingly, the abortion rate is 10 to 12 thousand per year (National Statistics office of Georgia), which is quite a big number for a country of 3.7 million. It must be noticed, that illegal abortions are, in fact, eliminated. The rest of the registered abortion rate has steadily positive dynamics, which means it is reducing. Here it must be noted that the main reason for this achievement in our country is the wide implementation of contemporary contraceptives by the Zhordania Institute. It may not be ignored that in this process, the representatives of local media were helpful, and are still helping us. We appreciate the Ministry of Health, Labor and Social Affairs of Georgia, which does not interfere in matters that we are in charge of.

The position of our Church is very important as well, which believes that abortion is a big sin and must be eliminated. My colleagues and I fully share this opinion and additionally, we believe that abortion is devastating to a woman's health and must be abolished. As for contraception, the Georgian Christian Orthodox Church, also, considers it as sin, but "less sin than abortion". That kind of assessment is, at this time, absolutely acceptable for us, the reproductologists, especially, because it does not make an accent on the abortion and its administrative prohibition or reducing the usage of contraception, which of course, is the result of our explanations, based on the facts of the world experience.

Today, there is no doubt in more or less competent specialists, that in the sphere mentioned above, any prohibition does not bring any result and does not change the abortion rate, but increases the number of illegal and nonmedical artificial abortions only. The later leads to an increase of maternal mortality and morbidity rates. This is evidenced by the bitter experience of

Post-Soviet countries, Romania, Ireland, Poland and others. Evidence shows that restricting the access to abortions does not reduce their number (Bearak et al. 2020). The proportion of unsafe abortions are significantly higher in the countries with highly restrictive abortion laws, than in more liberal ones (Ganatra et al. 2017). Besides, paradoxical is the fact, that the administrative prohibition of abortion causes the rising of so-called Gynecological Tourism. The women, for the need and reason of abortion, travel to other countries, where the procedure is permited. In addition, the world study showed, that in countries where abortion was restricted, the proportion of unintended pregnancies, ending in abortion, had increased, but it decreased in countries where abortion is broadly legal (Bearak et al. 2020).

Our colleagues and we think that abortion must not be prohibited, but eliminated. This must happen by introducing modern contraceptives, comprehensively informing the population and adequately educating it. Until abortion remains the reality of our life, talking about its prohibition is detrimental. It is necessary to speak about the harm it brings to a woman's health. At the same time, temporary introduction of modern alternatives of artificial abortion is necessary. In Georgia, such a temporary alternative has become the so-called Mini-Abortion (Vacuum Aspiration Procedure), which was much harmless for the woman's health compared to traditional surgical abortion. It has played its role, but by 2000, my colleagues and I decided, that Mini-Abortion has run out of steam. That's why we introduced Medical Abortion, which is less harmful for the women, less expensive and not needing hospitalization.

Our consideration of any type of abortion is clearly negative, and it must be eliminated totally, but not by the prohibition and forcefulness, but only by means of explanation, interpretation, promotion of relevant knowledge and education.

We are absolutely sure, that if there is anyone who hates abortion, that's us, the doctors of the field of Reproductology, in the first place. The reasonable position of the Georgian Association of Reproductive Health is that in the latest years, the attitude of our country towards abortion and family planning is absolutely fair and right, and should be continued as long as the results are evident.

We are often asked: is abortion a murder? My colleagues and I answer with firm determination: Yes, abortion is murder, because human life begins from its conception. This kind of answer is conducive to the second, natural question: should the killing doctors, who carry out abortions, be punished? Our definite answer is: "No", if the doctor carries out the procedure absolutely altruistically, only when he is sure that the patient has the vital, medical and social contraindication for pregnancy. Besides, the doctor must explain to the patient everything to persuade her in pregnancy maintaining.

In fact, all this does not relieve the doctor from murder responsibility!

Because of unfair situation, after a long thinking, my colleagues and I formed our philosophy of antenatal life, with the hope that someday, simultaneously with elimination of abortion, the practical necessity of mentoned philosophy will disappear.

Probably, needless to say, that we are not comforting ourselves or imposing our opinion on anybody.

Nevertheless, let us introduce our thoughts on theoretical and practical assessment by the readers.

As already mentoned, we accept the suggeston that all types of artfcial aborton are thought to be the facts of life terminaton and murder, but it must also be noted that in our opinion, life is of two types: antenatal and postnatal. The postnatal life begins afer delivery and it totally belongs to the newborn. Artfcial interrupton of this life is the greatest crime and is judged accordingly. As for the antenatal life, it difers qualitatvely from the postnatal life, frstly because it belongs not only to the fetus, but also to the mother. As the fetus is not capable of making a decision, before God, the responsibility for the sin must be placed on the mother and not on the doctor, who is forced into making an aborton. Is it necessary to judge the mother for the crime or not, is a separate issue. We think, that artfcial aborton is the mother's sin, but not the crime and only God can judge its level.

Presumably, everybody agrees that there are many such facts in our lives, the fair defniton of which exceeds our thinking ability. The rank-and-fle are not capable of analyzing such facts, but put their trust into God's will. One of them is the stll existng aborton.

We have been clarifying repeatedly, that the theory, mentoned above, is the product of our subjectve thinking, which we are not imposing on anybody. We want you, our dear readers and colleagues, to give consideraton to the fairness and objectvity of our theory.

Conclusions:

1. Aborton should be eliminated, but not prohibited or restricted;
2. Informing the populaton of modern contracepton and its educaton in this connecton must be made essental;
3. Aborton is certainly a murder, but in this partcular situaton, it is a sin rather than a crime;
4. Considering our theory about dividing the life into "Antenatal" and "Postnatal" types, all the sin of aborton should be placed on the mother, but not on the doctor.

Declaratons of interests We declare no competng interests.

Acknowledgements

We alone are responsible for the views expressed in this artcle, and they do not necessarily represent the views, decisions or policies of the instttutons with which they are afliated.

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PREIMPLANTATION GENETIC TESTING (PGT) FOR LATE ONSET GENETIC DISEASES

Preimplantation genetic testing (PGT) for late onset genetic diseases raises moral and ethical argument for its application. Although some health care providers find it just fable, others dispute it.

The genetic variant of Creutzfeldt–Jakob disease (JCD) which is one of the known late onset diseases can be prevented by using PGT. Approximately 15% of JCD are inherited disorder associated with PRNP gene mutations. This is an autosomal dominant late-onset neurodegenerative disorder with nearly 100% penetrance, and is prevalent among Jews of Libyan descent having a common PRNP E200K founder mutation. Many young patients at risk for CJD prefer not to know their genetic status but still do not want to pass on the mutation, if it exists, to their offspring. PGT or Prenatal diagnosis through direct mutation analysis force them to learn their own carrier status. A solution for such problem is referred as “testing by exclusion”. By this method the embryos are tested for the non-presence of any allele of the relevant gene from the affected grandparent. This procedure is designed to avoid the birth of at-risk offspring to an individual who chose not to perform a predictive test.

Dr. JENARO KRISTESASHVILI
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CHROMOSOMAL ANOMALIES IN COUPLES WITH RECURRENT PREGNANCY LOSS

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2. Center for Reproductive Medicine "Universe",
3. Georgian Centre of Prenatal Diagnostics.

Background

Genetic factors are the most common causes of spontaneous abortions (SA); Numeral chromosomal anomalies (aneuploidy or polyploidy) are observed in 50-80% of I trimester abortuses, depending on investigation methods used (FISH, CGH microarray, etc.), investigated groups composition (advanced age of women), peculiarities of family or obstetric history, etc (1,2). Most chromosomal abnormalities that cause miscarriage, have random character and mostly (90%) are expressed by I trimester SA, however these abnormalities might be associated with RPL (3,4).

Frequency of chromosomal abnormalities in couples with RPL is 2-6% according to different data (1,5,6). Translocation in one of the partners is common and confirmed cause of recurrent miscarriage (7,8). Prevalence of balanced translocations is higher in females than in males and higher in couples with family history of stillborn or abnormal liveborns and according to some authors in subfertile men (1,3,9,10).

On the basis of meta-analysis of 79 studies, Tharapel A.T. et al. revealed that among couples with RPL the structure of identified chromosomal abnormalities is as follows: either partner of couples with RPL has balanced reciprocal translocation in 50%, Robertsonian translocation – in 24%, sex chromosome mosaicism – in 12% and in other cases inversions and different sporadic chromosomal abnormalities were observed (11).

The presence of a balanced chromosomal rearrangement in one partner can result an unbalanced translocation in offspring. Phenotypic consequences (abortuses or abnormal liveborns) depend on the specific duplicated or deficient chromosomal segments (1,2,5).

Translocations don't correlate with the age of mothers and number of previous miscarriages (1,6,12).

Theoretical risk of transmission of balanced translocations to offspring in unbalanced form is considerably higher than empirical risk, that might be explained by lethality of many segregant products (1,5,6,8).

In cases of translocations different chromosomal aneuploidy may be expressed as a result of interchromosomal effect (1,13). In I trimester abortions recurrent aneuploidy occurs more often than expected by chance, that might be tied to age of mother and also to germ cell mosaicism (1).

According to the last period data, in cases of structural abnormalities of chromosomes, IVF accompanied with PGD decreases the risk of spontaneous abortions, but also decreases the chance of live birth compared to spontaneous pregnancy. In cases of spontaneous pregnancies, taking into account concomitment factors, live birth chance is up to 70% (2,5,12).

There are no common views on necessity of karyotyping of conceptuses, also in which cases karyotyping of couples with RPL (RCOG, ASRM, ECHRE protocols) is economically justified (14,15).

According to some experts' opinion, karyotyping of couples with RPL is recommended if there is no information on karyotype of conceptuses (15,16).

Objective

Detection of frequency and types of chromosomal anomalies in couples with I trimester RPL without the history of delivery with abnormal fetus.

Material and Methods

122 couples with > 2 first trimester miscarriages were involved in prospective observational study in 2014-21 on the basis of Center for Reproductive Medicine "Universe" and Georgian Centre of Prenatal Diagnostics;

Mean age of women was 30,3+2 and mean age of men – 32.1+3

In all cases family history and obstetric anamnesis have been collected and analyzed;

Common causes of RPL – anatomic (congenital and/or acquired), hormonal (lutheal insufficiency, diabetes, thyroid dysfunction, PCOS, hyperprolcatnemia, etc), immunological (APS) were excluded for all couples;

All couples have undergone cytogenetic investigation. Detection of karyotype was performed in peripheral blood lymphocyte cultures (G-banding).

Ethical considerations

A written consent form was signed by all the participants.

Results and discussion

Personal or family history of pregnancy and delivery of fetus with congenital anomalies or child with mental retardation was not detected in none of cases;

Karyotype of previous conceptuses was not investigated in none of cases;

Mean number of previous miscarriages in common group of RPL was 3,15 and in the couples with chromosomal anomalies – 2,9;

Chromosomal anomalies in one partner were revealed in 10 cases (8.2%); (Tabl.1)

Balanced reciprocal translocations were detected in 4 men and 2 women (Fig. 1), Robertsonian translocation – in 2 man, 3 from 6 men with translocations (2 Robertsonian and 1 reciprocal) were subfertile (olygozoospermia);

Total frequency of balanced translocations was 6,6% (8);

One woman had pericentric inversion of chromosome 9 and one woman – mosaic karyotype 46, XX/47, XXX.

Pericentric inversion of chromosome 9 was revealed in 1 woman with a history of 3 previous I trimester spontaneous abortions, karyotype – 46, XX, inv (9) (p 11; q12);

Pericentric inversion of chromosome 9 is considered as a variant of normal karyotype with incidence 1-3% of general population (17). This inversion doesn't correlate with abnormal phenotypes, but in literature exist conflicting views regarding association of this variant with such clinical conditions, as infertility, RPL, stillbirth (17,18,19).

Mosaic karyotype 46, XX/47, XXX (37/63) was revealed in 1 woman with a history of 3 previous I trimester spontaneous abortions. Sex chromosome polysomy is very rare (0,05%) among spon-

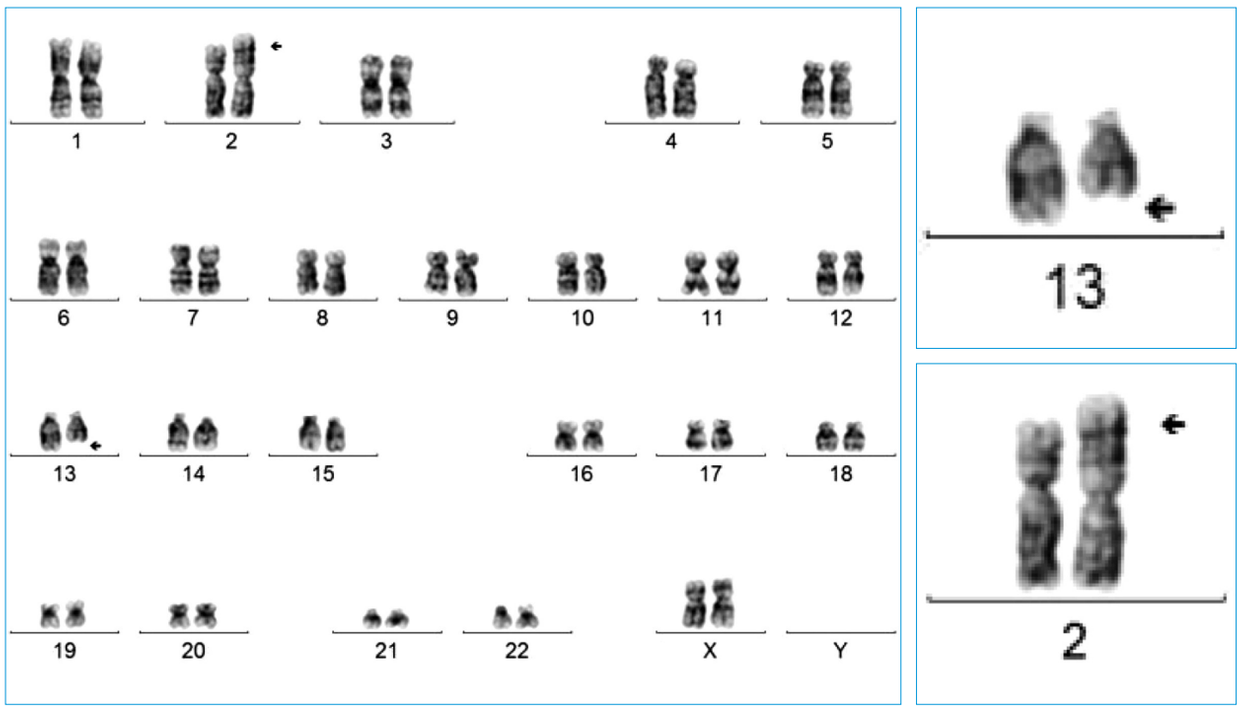

Fig. 1. Couple with 2 SA Woman 21y old, Karyotype 46, XX, t (2;13) (p14;q32)

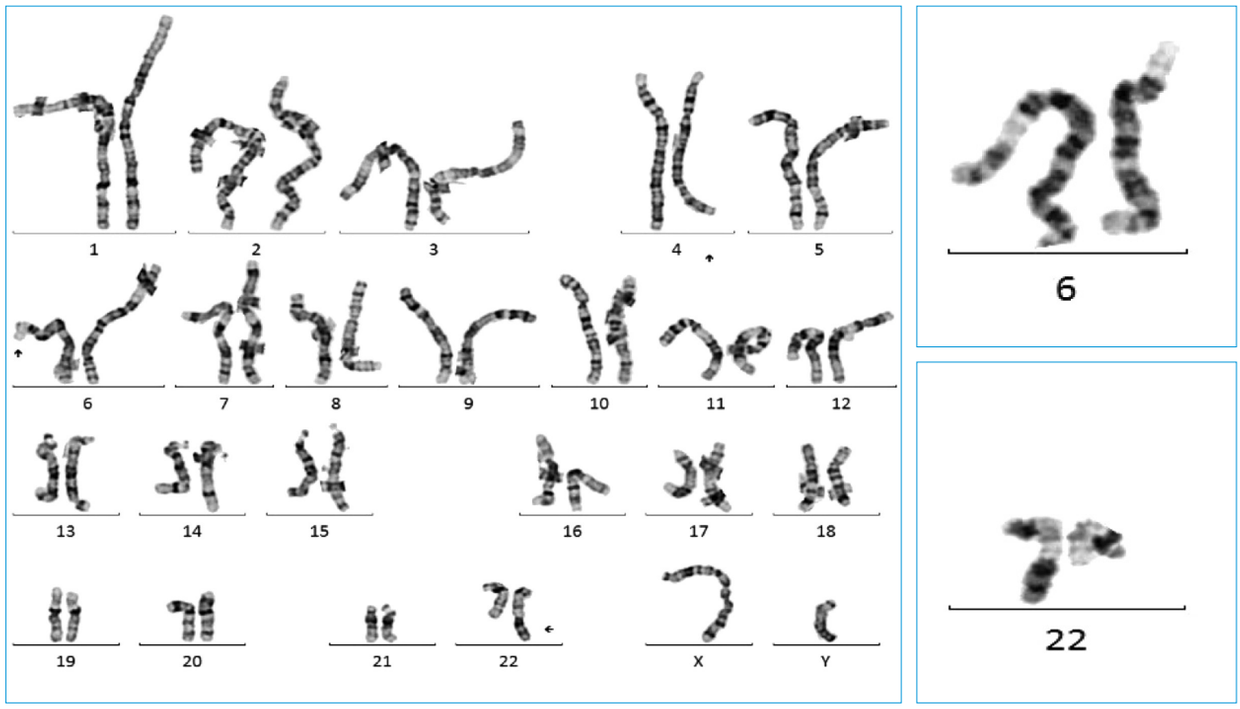

Fig. 2. Couple with 4 SA Male partner 30 y, old, Karyotype 46, XY, t (6;22) (p21.3;q13.3)

taneous abortuses and it is not a conditon, incompatble with life (1). Thus, causatve relaton of pericentric inversion of chromosome 9 and X chromosome polysomy with RPL needs further investgaton.

Genetc counseling has been conducted for all couples with detected chromosomal anomalies; These couples were informed regarding their risks and reproductve opportunites:

- IVF accompanied with PGD;
- Spontaneous pregnancy or IVF with or without CVS or amniocentesis;
- Donaton of gametes;
- Adopton of a child.

Finally, couples have made their decision on using above-mentoned opportunites.

Afer investgaton and detecton of chromosome anomalies and genetc counseling, 2 women became pregnant (spontaneous pregnancies);

One 24 y. old woman (who's 26 y. old husband had reciprocal translocaton 46,XY,t(6,22) (p21.3;q13.3)) (Fig. 2) with the history of 4 previous I trimester spontaneous abortons, became pregnant spontaneously and was under intensive prenatal care and psychological support, results of noninvasive prenatal genetc screening (biochemical and US) were in the frame of norms; The pregnancy ended with a tmely physiological delivery, a phenotypically normal girl was born with a normal karyotype 46,XX.

Another 39 y. old woman with the history of 2 previous I trimester spontaneous abortons, had reciprocal translocaton 46, XX,t(5;16)(p12;q22), also became pregnant (spontaneously). On 18th week of pregnancy fetal balanced translocaton (similar to maternal) was detected by amniocentesis. Physiological pregnancy was maintained and ended by physiological delivery with phenotypically normal fetus.

Revealing of real causes of RPL by karyotyping of couples, might be beneficial for these couples as well as for experts, involved in management on this problem.

The results obtained by us indicate that the karyotyping of couples with RPL without the history of delivery with abnormal fetus is reasonable, because chromosomal anomalies among them is not so rare (8,2). Balanced chromosomal rearrangement in one partner can result an unbalanced translocation in offspring and phenotypic consequences (abortuses or abnormal liveborns) depend on the specific duplicated or deficient chromosomal segments (1, 2). In some cases, the above mentoned chromosomal disorders can be clinically revealed mainly by spontaneous abortions(3, 13).

In cases of chromosomal anomalies, the couples with RPL have to make decision on their further reproductive plans, based on own opportunities and comprehensive information regarding the possibilites and risks received by genetic counseling;

Each country has to define indications for karyotying of couples with RPL due to country-specific peculiarites of health care system (whether the karyotyping of conceptuses is mandatory or not, accessibility to PGD, etc.) and financing sources of these investigations (14,15,16).

Conclusions

In the couples with RPL and without the history of delivery with abnormal fetus, when chromosomal status of previous miscarriages is unknown, considerable frequency of balanced structural chromosomal anomalies (with prevalence in male partners- 6/2) indicates on reasonability of karyotyping of such couples, especially when male partner is subfertle;

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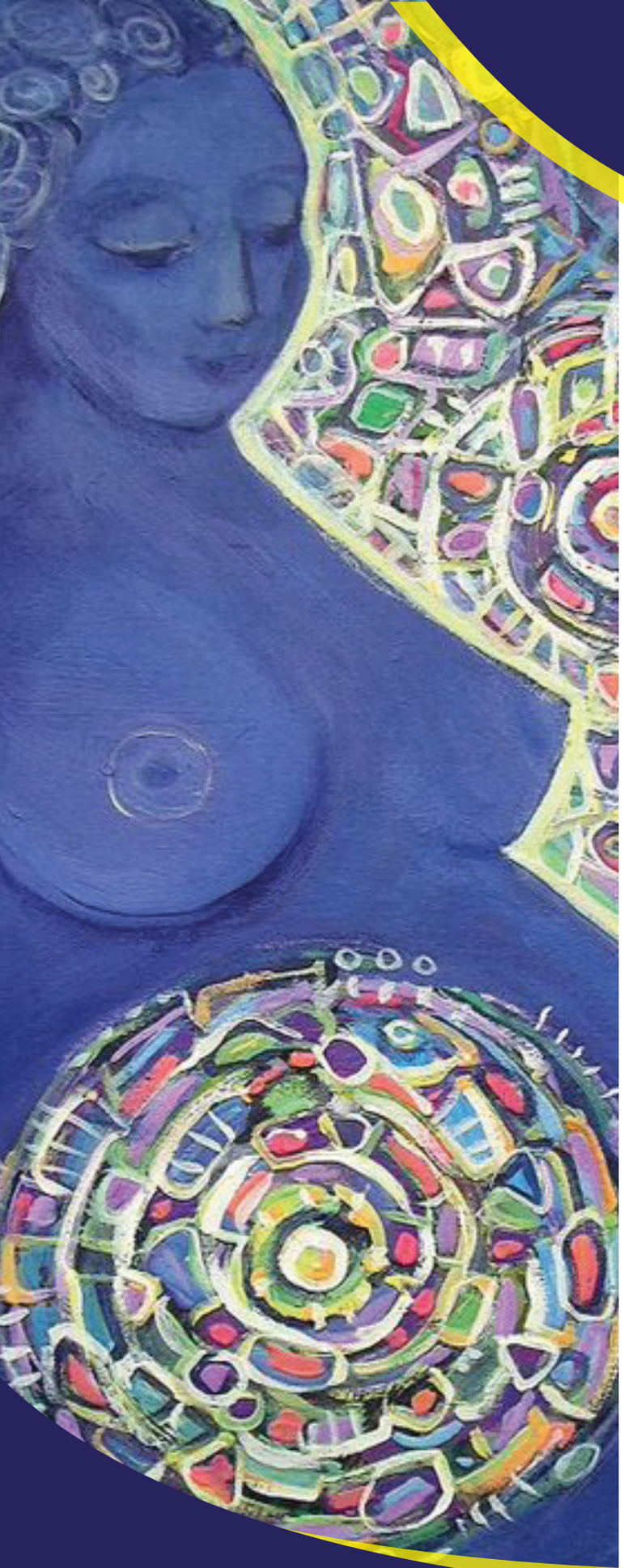
N	Karyotype	Numbers of first trimester miscarriages	Other reproductive disorders
1	46, XX, t (2;13) (p14;q32)	2	
2	46, XX, t (5;16) (p12;q22)	2	
3	46, XY, t (2;9) (p22;p24)	2	
4	46, XY, t (18;21) (q22;q21)	3	
5	46, XY, t (10;18) (q11,2; q2,1)	3	subfertlity (olygozoospermia)
6	46, XY, t (6;22) (p21.3;q13.3)	4	
7	45, XY, rob (13;15) (q10;q10)	4	subfertlity (olygozoospermia)
8	45, XY, rob (13;14) (q10;q10)	3	subfertlity (olygozoospermia)
9	46, XX, inv (9) (p11;q12)	3	
10	46, XX / 47XXX (18/32)	3	

Tab. 1. Type of Chromosomal Anomalies and Reproductive disorders in couples with RPL



GGRC

GGRC Ambulatory service is a concept that combines 'one stop' clinics and 'day surgery' operations as an alternative to traditional out patient consultations and in patient surgery. We issue here an advancing women and men reproductive health care.

- **Infertility treatment**
- **Screening and treatment of gynecological disorders**
- **Treatment of endometriosis**
- **Congenital disorders of reproductive system**
- **Sexually transmitted diseases**
- **Diagnosis and treatment of cervix uteri pathology**
- **Colposcopy**
- **Microscopic and computer-assisted diagnosis of testicular fluid**
- **Pregnancy monitoring**
- **Sonohysterography**
- **Endocrine gynecology**
- **Aesthetic endocrinology (hirsuties, acne/seborrhea, overweight)**
- **Neuroendocrinology (climacteric and premenstrual syndromes)**
- **Application of mechanical intrauterine devices (coil)**

AND THE MAIN DIRECTION OF THE CLINIC - CONSERVATIVE, OPERATIVE AND ASSISTED REPRODUCTIVE METHODS, INTERNAL INSEMINATION OF THE UTERUS AND IN VITRO FERTILIZATION, STEM CELL AND PRP THERAPY

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New Word in
Reproductive Medicine

- Foreign partners of GGRC are leading specialists from Germany, Israel, Turkey, Russia, Belarus and Ukraine, Georgian patients can consult online with them. The clinic uses modern methods of treatment and relies on the guidelines of European clinics.

- Clinic GGRC actively cooperates with foreign companies working in the field of medical tourism. There is a surrogacy-donation program on the basis of the clinic, which connects Georgian surrogate mothers with foreign childless couples.

- Corporate Social Responsibility of the clinic is the charity fund “For You”, which helps Georgian childless couples with co-financing program for In vitro fertilization.

- GGRC is the first and only clinic among the reproductive clinics in Georgia, which obtained the ISO standard, holds the license of the American laboratory quality standard FDA and is accredited by the Israeli Ministry of Health.

Together for new life!

Dr. H. ERAY COPCU
MD

SUPERCHARGED MECHANICAL STROMAL-CELL TRANSFER (MEST)

Summary

PRP and fat-derived stromal cell applicatons are the 2 most commonly used methods in regenerative medicine. PRP has a wide spectrum of indicatons. Mechanical methods have become very popular recently in fat-derived stromal cell applicatons due to the advantages they provide. Combining these 2 methods has produced more successful results. To date, this combinaton has been in the form of combining 2 products obtained separately just before they are administered to the patent. In this study, fat tssue and blood samples obtained from eight volunteers were mixed with PPP as a new idea not previously reported in the literature, and stromal cells were obtained mechanically with sharp blades (adinizing). Later, the obtained PRP was added to the fnal product and became "supercharged." The results were tested by the dual fuoroscopy method for cell number and viability, and the results obtained were analyzed statstcally. By adding the plasma to the oil before stromal cells were obtained and cu t ng with sharp blades by mechanical separaton, twice the volume and 4.7 tmes more cells were obtained compared with that obtained in the saline group ($P < 0.001$). We believe that the reason for this is the "binding" efect of the proteins in the plasma. This approach provided a higher cell count by using PPP, which is a "waste product," and in additon, the potental e f ciency was increased by adding PRP. However, the clinical results of this innovative method should be evaluated with advanced clinical studies. (Plast Reconstr Surg Glob Open 2021;9:e3552; doi: 10.1097/GOX.0000000000003552; Published online 10 May 2021)

Introduction

In many medical disciplines, regenerative medicine has recently been a fast-growing and popular trend. The use of fat-derived stromal cells and blood-derived plateletrich plasma (PRP) is one of the most common applications.[1] Stromal cells are obtained mechanically rather than enzymatically, not only because of legal restrictions but also because such procedures are easier and are capable of obtaining more cells efficiently and economically.[2] Obtaining stromal cells from adipose tissue by enzymatic method has been described elsewhere in detail.[3] To date, many devices have been applied in different ways, but consensus has yet to be reached on the definiton of the final product or even the preparaton protocols in mechanical ways.[4] Copcu and Oztan, in their study published in 2020 on using sharp-knife systems, obtained a high number of stromal cells mechanically without creatng blunt-force pressure.[2] The name they gave to the procedure of cutng fat tssue with a sharp knife was "adinizing" and represents the frst tme indicaton-based protocols were established for the final product, its desired physical structure (solid, liquid, emulsified), and the required number of cells. Unlike enzymatic methods, they suggested that the term total stromal-cell (TOST) should be applied to the final product, instead of stromal vascular fracton (SVF).[4] PRP, on the other hand, has a much longer history than stromal cells, and many methods are used successfully in terms of the efects of growth factors on wound healing and regeneraton.[5] In this study, as an innovative alternative to the saline soluton used in the indicaton-based protocols, the process of cutng with sharp blades (adinizing) was performed by combining platelet-poor plasma (PPP) and condensed fat. Thus, by using plasma stromal as a "binder" for cells, the aim was to obtain more cells and greater volume.

Material and Methods

This study was conducted according to the standards of good medical practce (ICH-E6) and the principles of the Declaraton of Helsinki. All patents were provided detailed informaton preoperatively, and they gave writen consent for all surgical procedures, anesthesia, intraoperative video recording, and photography. In additon, a writen consent form was obtained from the patents statng that they willingly donated their adipose tssue for laboratory analysis. In this study, a patented CE marking, and ISO 13485 certfed blade system was used, and rules of minimal manipulaton were followed. No enzymes and similar chemicals were used, and the structure of the fat tssue was not altered. A TriCell PRP kit (Rev-Med Inc, Korea) was used to obtain PPP. Twenty-seven cm3 of venous blood was mixed with 3 cm3 citrates. It was frst centrifuged at 3200 rpm for 4 minutes, then at 3300 rpm for 3 minutes, and afer the second centrifuge, the PPP in the second chamber of the kit was automatically obtained. Under local anesthesia, 15 cm3 of adipose tssue was harvested from the abdominal area with a 3-mm-diameter 4-hole cannula and then centrifuged at 500 G for 2 minutes, and condensed fat was obtained by discarding tumescent fuid and blood elements. An estmated 5 cm3 condensed fat was mixed with 5 cm3 PPP in the study group and 5 cm3 saline in the control group, and then the adinizing process was performed with 2400-µm, 1200-µm, and 600- µm diameter ultra-sharp blades, respectively (Adinizer, BSL-rest, Korea) with 25 back-and-forth movements between the 2 injectors. Finally,

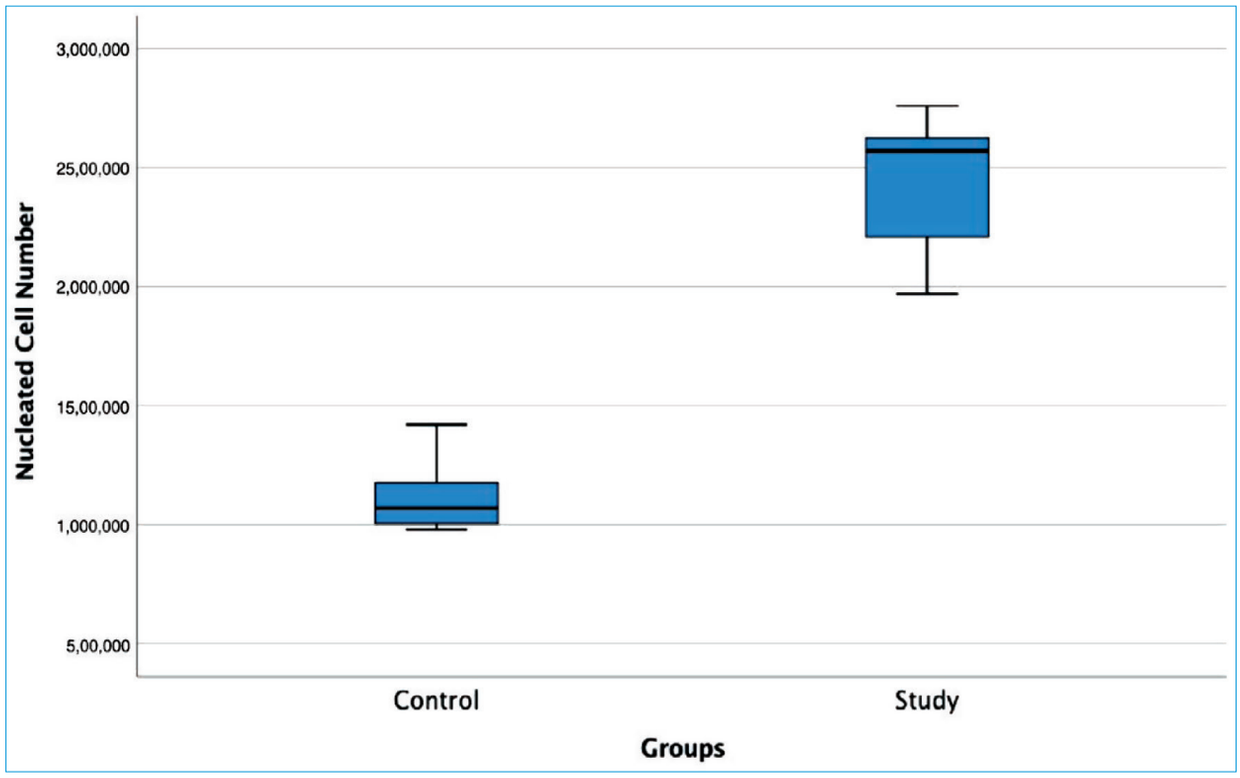

Fig. 1. Comparison of nucleated cells in milliliters. While an average of 1.11 x 106 ± 1.46 × 105 nucleated cells were obtained in the control group, this number was 2.44 x 106 ± 2.99 × 105 in the study group. The 2.2-fold difference between them was found to be statistically significant (<0.001).

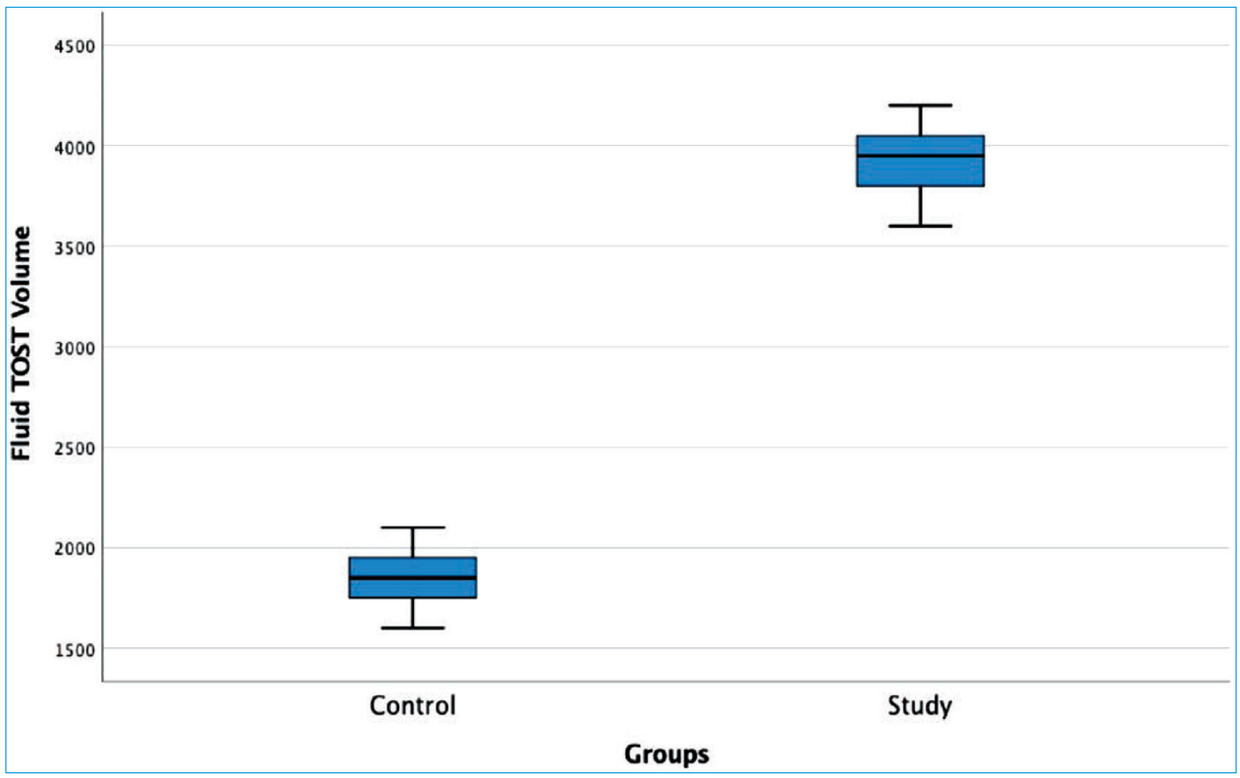

Fig. 2. Comparison of volumes of total stromal cells (TOST). While an average of 1.85 ± 0.16 mL TOST was obtained after the procedure in the control group, this volume was 3.92 ± 0.19 mL in the study group. The 2.1-fold difference between them was found to be statistically significant (<0.001).

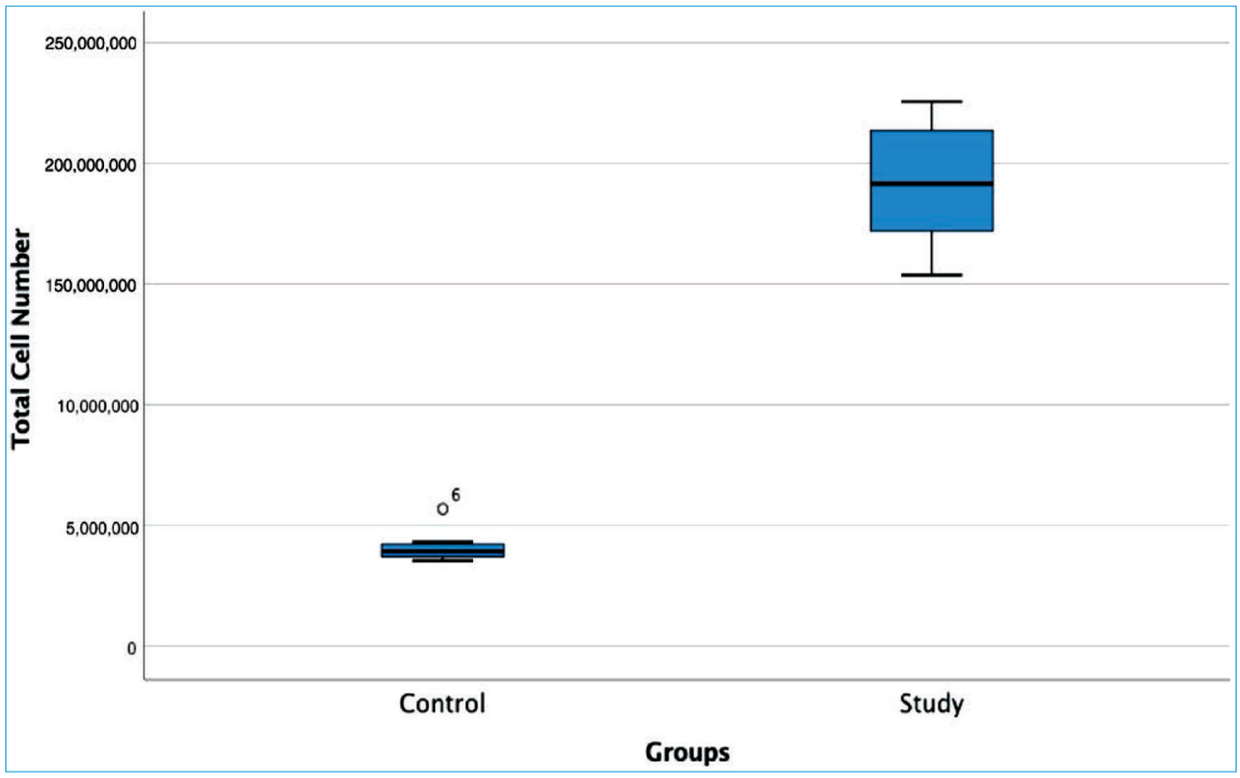

Fig. 3. Comparison of total nucleated cells in 10 mL condensed fat. When 10 cm3 of condensed fat tissue was taken as reference in the control group, an average of 4.11 × 106 ± 6.78 × 105 stromal cells were obtained after all procedures, while this number was 19.16 x 106 ± 2.58 × 105 in the study group. The 4.7-fold difference between them was found to be statistically significant (<0.001).

stromal cells were obtained by centrifugation at 1200 G for 5 minutes. The final product, total stromal cells (TOST), was obtained mainly in liquid form. (**See Video [online],** MEST preparation.) Total viable nucleated cell recovery and the viability percentage were determined using a LunaStem Automated Fluorescence Cell Counter device (Logos Biosystems, South Korea) with acridine orange/propidium iodide stain in each delivery method before and after the process. After the process was completed, PRP was added to TOST. Thus, stromal cells were obtained from adipose tissue mechanically by using PPP simultaneously, and a much stronger effect was expected by adding PRP obtained from blood to TOST.

Results

Supercharged mechanical stromal cell transfer (MEST) was tested in 8 cases, and results are presented in Figures 1-4. Components of whole blood and adinized fat after centrifugation are presented in Figure 5.

Discussion

When PRP is obtained in conventional applications, the plasma part (called PPP) is discarded, and the PRP part is applied in a wide spectrum due to the growth factors it contains.[5] The clinical application of PRP by combining it with stromal cells obtained from adipose tissue both enzymatically and mechanically is not a new concept.[1,5-7] Stevens et al described this approach as plate-

let-rich stroma and reported that it would yield more successful results in androgenic alopecia and osteoarthritis than PRP alone or SVF alone.[1,6] Similarly, Butt et al obtained stromal cells from adipose tissue mechanically and emphasized that in its combination with PRP, it provided results far superior to the sole use of PRP.[7] Our study differs from all stromal cell PRP combinations in the literature.[1,5-7] In our study, for the first time, we obtained stromal cells from adipose tissue by mixing 50% of the condensed adipose tissue with PPP before the procedure, mechanically using sharp blades. In the technique described previously by Copcu,[2] indication-based protocols were

	Control group	Study group	P
Nucliated Cell Number in ml.	1,11 x 10^6 ± 1,46 x 10^5	2,44 x 10^6 ± 2,99 x 10^5	<0.001
Fluid TOST Volume ml.	1,85 ± 0,16	3,92 ± 0,19	<0.001
Total Nucliated Cell Number in 10 cc Adipose Tissue	4,11 x 10^6 ± 6,78 x 10^5	19,16 x 10^6 ± 2,58 x 10^5	<0.001
Viability (%)	92,25 ± 3,19	92,13 ± 1,56	0.922
Average Nucleated Cell Size (µm)	9 ± 2	8 ± 3	0.896

Fig. 4. Comparison of results of control and study group (The data analysis was carried out using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, N.Y.). The descriptive statistics were given as mean ± SD. The normal distribution of the numerical variables was determined by using the Shapiro-Wilk normality test. If the data complied with a normal distribution, the statistical differences between the groups were evaluated using the 1-way analysis of variance and post hoc tests. If the data did not comply with a normal distribution, Mann-Whitney U tests were used. A P value of <0.05 was considered to be statistically significant.) In the study group, 2.2 times more nucleated cells were found in 1 mL (<0.001). As a result of the process, TOST was obtained at 2.1 times higher volume (<0.001). When 10 cm3 of condensed adipose tissue was taken as reference, a total of 4.7 times more stromal cells was obtained (<0.001). There was no statistically significant difference in viability and average cell size in the study and control groups (0.922, 0.896).

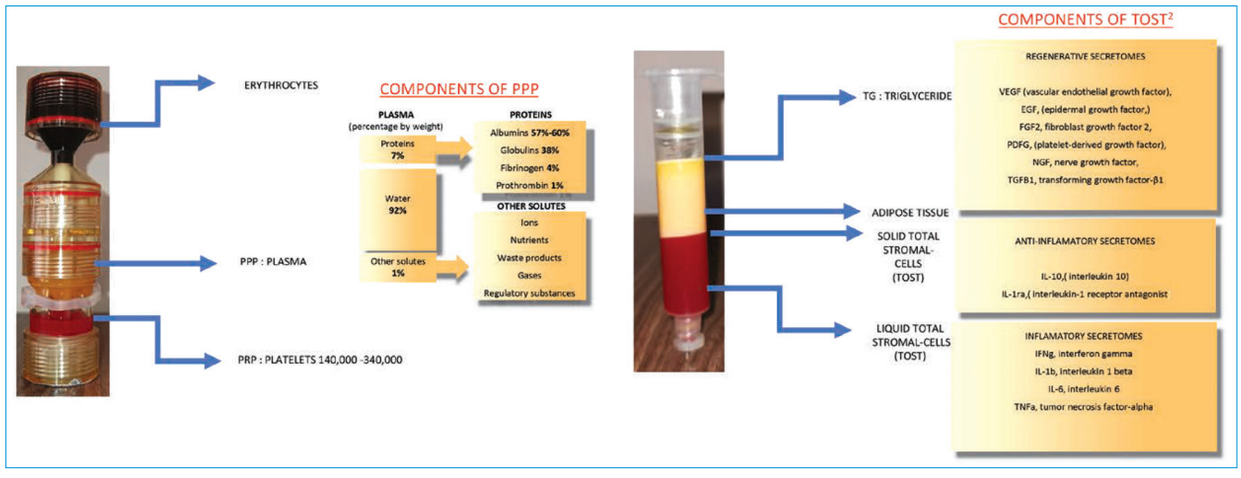

Fig. 5. Components of whole blood and adinized condensed adipose tissue after centrifugation.

defined to obtain a higher number of stromal cells in liquid form (conventionally, they are in solid or emulsified fatty consistency) by mechanical stromal cell recovery processes. In this approach, when the adipose tissue was mixed with saline at a rate of 50% before adinizing, more cells and total stromal cells were obtained in liquid form. It has been speculated that possible reasons for this may be polarity and density. Adipocytes have no positive and negative charged points – the charge distribution is equal, indicating that they are nonpolar. Molecules that are nonpolar do not dissolve well in polar structures such as water; they tend to repel each other and remain separated, even when shaken vigorously.[8] However, mesenchymal stromal cells respond to superficial electric charges, unlike adipocytes.[9] With the back-and-forth movements described above, the stromal cells are released when the adipose tissue passes through the metal blades between the 2 injectors. However, the kinetic energy generated at this time affects the polarity of the cells. We believe that in pre-adinizing dilution, this electrical polarity affects the relationship between saline and stromal cells and helps separate stromal cells more successfully. Also Zimmerlin described intra-tracheal route of stromal cells combining with fibrin as a kind glue.[10] In the innovative approach we are presenting in this study, plasma is used instead of saline. The content of plasma is 7% protein and 4% fibrinogen. We argue that thanks to these structures in the plasma acting as a binder for stromal cells, it is possible to obtain both twice the volume and 4.7 times more stromal cells.

Conclusions

We think that at the same time, the addition of the obtained PRP to this final product will allow the application of “supercharged” cells in a much stronger sense, as described in many studies in the literature. However, advanced clinical studies are required to prove this hypothesis.

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CURRENT ADVANCES ON CARRIER SCREENING AND AN INNOVATIVE APPLICATION: CARRIER CHECK

It is estimated that there are more than 1800 inherited RDs varying in frequency across geographic areas, due to population genetic diversity, environmental or societal factors or survival rates1. In Europe, 12 RDs account for 90% of all cases2, according to Mikrogen's own PGT-M data consisting of ~2500 patients from Turkey and Middle Eastern countries, the overall rate of these same 12 diseases remains at 35%. Due to high consanguinity rates, rare heterozygous conditions manifest as homozygous resulting in offspring affected with rare or novel syndromes.

Europe is becoming increasingly heterogeneous, with growing proportions of individuals reporting mixed ancestry, increasing numbers of mixed ethnicity couples and migration waves3. Currently, there are 3.6 million registered Syrian refugees in Turkey4 and 320.000 refugees from other nationalities (Iraqi, Afgan, others) are also registered5. The Turkish Statistical Institute states that 30% of Syrian refugees are at the reproductive age and in the last four years 518.730 refugee new-borns were recorded6. In 2019, 27 million people migrated to Europe, 21% of whom are from Middle Eastern countries7.

Due to continuous migration, high reproductive rates and consanguinity of Syrian refugees, the fight against rare diseases has gained a new dimension for Europe as a public health priority8. Unknown genetic variants of common RDs and novel syndromes are being introduced into the genetic make-up of Europe and expected to increase in frequency in the short-term. Preconception screening is a crucial component of preventing the future generations from RDs.

This points to the need for a screening test covering the most prevalent diseases without compromising test sensitivity and being able to detect diverse variants from European and Middle Eastern genetic pools in order to respond to the diversity of a geography becoming more and more multi-ethnic and multi-cultural.

Majority of preconception screening tests report only Class I and II variants which are pathogenic (99% certainty) or likely pathogenic (90% certainty) respectively, to stay on the safe side. But carrier status information of an RD can be carried on a novel variant, even if the susceptibility gene is well studied and pathogenicity of the variant is not clear yet. Thus detection and interpretation of Class III variants, namely variants of uncertain significance (VUS), which can also be detected on unlikely regions of the genome, like intronic and deep intronic regions, require additional analysis and interpretation attention.

There are also certain regions in the genome, which are challenging to cover both by wet-lab and in-silico techniques. Regions containing pseudogenes (i.e CYP21A2), chromosomal mutations (i.e deletions, duplications) or CNVs require special attention due to potential overcalls (false positives) or loss of detection precision when using an NGS based test. Conventionally these problems are overcome by performing additional tests such as MLPA, bringing in additional costs.

Population-based databases provide information on the variant frequencies for RDs but certain ethnic populations, age groups, and genders remain under-represented. Therefore, how many of the >1000 known AR conditions should be included in an ECS panel still is a topic of considerable debate10. Carrier Check's concise gene and target content will be selected using a comparative and integrative gene selection method scanning various sources of existing ECS tests and in-house registry data.

ECS panels include a collection of causative genes with differing technical difficulty in detecting genetic variants, residing in both coding and non-coding regions. Gene panel design should take a comprehensive perspective on the properties of included genes facilitating gene-capture tool selection, sequencing depth determination, and dedicated data analysis2. For assay and analysis pipeline development an integrated and iterative workflow will be followed.

Detecting variants in complex regions in the genome requires multiple workflows and assays. For technically challenging variant types, novel solutions will be developed and tailored to the assay based on Genoox's proprietary machine-learning based bioinformatic tools, both by algorithm design and model training. The methods will be thoroughly validated as part of this project using orthogonal methods.

Variant classification is not always a solid information; classification of a variant can change depending on the accumulated data. Moreover classification of a variant can differ among different databases and the reporting decision of a VUS can be problematic. To tackle this problem, Carrier Check will be integrated with Genoox's cloud based public interpretation tool.

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KEY ASPECTS OF PREIMPLANTATION GENETIC TESTING (PGT)

Preimplantation Genetic Testing (PGT) includes Preimplantation Genetic Test for Monogenic Disorders (PGT-M) , Preimplantation Genetic Testing for Aneuploidy (PGT-A) and Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR) . Each of these PGT approaches have unique crucila points that can alter confidence , applicability and efficiency of the test.

PGT-M for genetic diseases that can be diagnosed has been applied for many years. Simultaneous monogenic disease testing and euploid embryo selection (combined PGT) has become possible with the development of Whole Genome Amplification (WGA) technologies. As a result of widespread use of whole exome/genome sequencing technologies, variety of single gene diseases referred for PGT-M has started to increase thus leading to a considerable elevation in the number of setup studies conducted for rare diseases.

Trophectoderm biopsy is widely performed for PGT-A, yet the efficiency of PGT-A results of different IVF centers show substantial variability. Most of the PGT-A samples are outsourced, commonly referred as transport PGT. In conjunction with the reported findings claiming that the potential discrepancies in the efficiency of Whole Genome Amplification (WGA) quality parameters of biopsy cells obtained from different centers might originate from the diversity in the techniques of biopsy practitoners.

PGT-SR for the detection of chromosomal rearrangements using Next Generation Sequencing (NGS) has been applied with a resolution of ≥ 5-20 Mb, which is the declared detection limit of commercially available kits. However, still some patents carry chromosomal rearrangements below the detection limit. Therefore, utlization of a customized analysis approach is required for the effective use of this technology for the detection of a broad range of chromosomal imbalances.

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NEW CHALLENGES OF ANEUPLOID EMBRYO TESTING BY NON-INVASIVE cFDNA

The high incidence of chromosome aneuploidy in human gametes and embryos is a major cause of in vitro fertilization (IVF) failure and miscarriage. In order to improve live birth rates with single embryo transfer, the use of preimplantation genetic testing for aneuploidy (PGT-A) has significantly increased. PGT encompasses methods that allow embryos to be tested for inherited conditions or screened for chromosomal abnormalities.

However, PGT relies heavily on invasive trophectoderm (TE) biopsy. The problem is that such biopsy procedure is often invasive and may hamper clinical outcomes as well as brings unknown health risks in long-term development of the embryos. Also, embryo biopsy requires specialized equipment and extensive expertise in embryo treatment, which is difficult to standardize and very challenging to meet the demand of performing in every IVF-eSET treatment. Therefore, there is no doubt that an effective non-invasive chromosome screening approach is highly demanded to prioritze embryo for transfer in the clinical practice of IVF-eSET.

Recent years, an increasing number of studies have been conducted to evaluate the feasibility of SCM-based niPGT-A approaches, and some of the results are encouraging. The success rate of cfDNA amplification and detection is high, ranging from 73% to 100%

In a clinical context, Rubio et al. compared the clinical outcomes of two groups of patients; one with both TE biopsy and SCM results of euploidy, and the other with TE biopsy-negative and SCM results of

aneuploidy. The transplant success rate of patents with both euploidy TE and SCM results was two-fold (52.9% vs. 16.7%) higher than that in the later group. Zero miscarriages were observed (0/9) when both the TE and SCM results indicated that the embryos were euploid. Moreover, a single-center clinical trial was conducted in 2019 using niPGT-A in patent groups with either repeated implant failures (≥3) or repeated miscarriages (≥3). The results of this trial showed a clinical pregnancy rate of 58% (29/50) and a spontaneous miscarriage rate of ~10% (3/29), with a total of 27 babies successfully delivered. While the scale of the above studies and clinical trials was small, cfDNA-based niPGT-A proved that, in principle, it could reduce miscarriage and improve the sustained pregnancy rate.

The current report focuses on the aneuploidy consistency between cell-free DNA (cfDNA) and embryos. However, the consistency comparison needs to consider many influencing factors, such as the definiton of consistency, sampling methods, analysis methods, etc.

We aimed to compare the advancements and limitaton non-invasive PGT (niPGT)-A. The more than 70000 tropheactoderm byopces has been done in NGC clinic in St. Petersburg and more than 40000 NGS test embryos in our NGC gen lab. So we our competence and experiance in PGT-A is enotugh. We had start to test cfDNA spent media since 2018.

We compared results of sequencing trophaectoderm 5-10 cells of blastocyst and cf DNA spent media same embryo for validaton reason at first. Then at moment 550 examinatons of cfDNA has been done in our practce for selecton embryo to transfer in IVF cycles. Non invasive testng has required different interpretaiton and aprouch according our experience. Mosaic results its concern moustly. So, in report will be present more detales, limitaton and peculiarites laboratory and clinicaly.

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DETERMINATION OF DNA DAMAGE FROM SPERM PREPARATION METHODS IN ICSI CYCLES AND MITIGATION WITH SPERM CHIP METHOD

Introduction

Almost 50% of all cases of infertility may be associated with a male factor. Still standard semen analysis does not provide any information about the genetic constitution of the sperm, which is essential for normal embryo development. Thus, a high level of DNA damage and aneuploidy of sperm cells may represent a cause of male infertility that conventional examinations cannot detect.

Therefore, sperm chips based on microfluidic channel mechanics appear to be a promising tool for a selection of physiologically competent sperm for fertilization, thus increasing efficiency of male infertility treatment. But does this method give any benefit in oocyte donation programs, or young and healthy oocytes are able to compensate sperm abnormalities by themselves?

Material and Methods

In order to assess the influence of sperm DNA fragmentation on development of embryos created from donor oocytes, fertilization and blastocyst formation rates were estimated retrospectively for two groups of cases from 2018-1019. Control group (n=40) included couples with

normal results of DNA fragmentation assay while patients whose sperm DNA fragmentation rate initially exceeded 30% were assigned to study group (n=40).

For the investigation of sperm chip efficacy, we compared results of oocyte donation cycles where fertilization was done with a sperm with high DNA fragmentation index. In the control group (n=50) sperm processing was done by density gradient centrifugation method, while in study group (n=50) sperm chip technology was used for sperm preparation.

DNA fragmentation of raw and washed sperm was tested with Halo sperm kit (Halotech). "Fertile" sorting chips were used for sperm processing. Fertilization was performed with ICSI-method. For every studied cohort fertilization, good blastocyst (AA, BA/AB and BB grades) and ongoing pregnancy rates were calculated.

Results

Investigation of sperm DNA fragmentation impact on donor oocytes ICSI results showed that in study group fertilization rate of donor cells was 77.2%, while in the group with normal sperm DNA fragmentation it reached 84.7% (NS, $p>0.05$). A significant difference in the blastulation rate after fertilization with sperm with different indices of DNA fragmentation was revealed as in the group with a high degree of sperm DNA fragmentation only 37.4% of zygotes formed blastocysts, while in the control cohort blastocysts rate was 51.2%.

While assessing sperm sorting chip efficacy, we noted 83.3% fertilization, 57.5% blastocyst formation and, after transfer of two embryos, 59.3% pregnancy rates in control group (mean male age – 33.7±4.2 years). In the study group (mean male age – 34.6±3.7), where sperm chip technology was used as the sperm preparation method, 90.4% fertilization, 68.3% blastulation and 70.4% pregnancy rates (pic.2) were achieved with a statistically significant difference for blastocyst rate and PR ($p<0.05$). Thus, usage of microfluidic sorting chips for sperm processing significantly increased probability to obtain blastocysts for transfer and freezing and gave a chance to expect more clinical pregnancies for couples with male infertility factor.

Conclusion

Since severe sperm DNA fragmentation negatively affects the embryologic step of IVF, careful sperm selection for fertilization may be a crucial step towards positive cycle result. As microfluidic sperm chips sperm selection supposedly enhances treatment effectiveness in terms of embryo development and clinical pregnancy rate, their use may be recommended for couples with damaged sperm DNA to increase efficacy of infertility treatment even in case of oocyte donation.

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WHEREVER YOU MAY BE, JUST WISH TO CARE!

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HUMAN ERROR MEASUREMENT AND HUMAN ERROR REDUCTION WITH ELECTRONIC WITNESSING SYSTEM (EWS)

Introduction

Human error in routine IVF can be measured with EWS. With our RFID chip EWS, human error can be reduced to very low levels. Existing studies show that electronic witnessing system works very successfully in all stages of IVF applications, but it is still insufficient in terms of cryopreservation and software. EWSs should secure all stages of IVF process from the time patient enters the clinic to the completion of all laboratory procedures. Our study is designed to ensure biological material safety with EWS and is intended to reveal statistical data of a system that can be actively used in all laboratory processes. We also determined the cryopreservation process and the performance of all IVF personnel with the system.

Material and Methods

15000 IVF cycles covering the years 2016-2020 were recorded with IVFID Electronic Witnessing system. Error warning received from 36 different IVF clinics were calculated and error distributions at each IVF stage were determined. Normal IVF patients within patient groups were registered as egg donation and surrogacy, and IVF stages affected

by human error were determined by calculating records of possible errors for each patient group. RFID electronic chip, electronic wristband and barcode system were used in every stage of patient groups. Thus, biological materials were secured throughout the entire laboratory process. The system recorded the data received via electronic chip through software and calculated it statistically. Human errors from each procedure in the embryology and andrology laboratories were recorded. In addition, the system was supported with personal witnessing patient software, and the error rate was reduced to zero.

Results

In our study, where 15,000 IVF cycles were evaluated, human error data received from 36 different clinics were evaluated and statistically calculated. Human error warnings were received 169 times out of 15,000 IVF cycles at different stages. Accordingly, error warnings were received 14 times during the oocyte pick up phase, 17 times during the denudation phase, 26 times during the ICSI phase, 8 times during the dish change phase, 68 times during the embryo transfer phase (17 of these were received during the fresh embryo transfer phase and 51 times during the thaw embryo transfer phase) and 36 times during the sperm preparation phase. When the error distribution according to different clinics were evaluated, error warnings were received from 23 out of 36 different clinics at different stages. Human errors were prevented by RFID electronic chip system and embryologist was warned visually and audibly on screens during the procedure. During the cryo phase of the IVFID Witnessing system with the vitrification straw chip system, no error warnings were received. Looking at individual embryologist performances, it is seen that error warnings were received from 32 different embryologists.

Conclusion

EWS‘s purpose is reducing human error and ensuring biological materials, safety. The use of system is important at every stage in Embryology/Andrology Laboratories. System can only send alerts regarding certain human errors, so 100% biological material safety isn’t guaranteed. Human factor will always exist, and individual witnesses should support EWS. Regular use of EWSs in IVF laboratories is very important to avoid human error-based interferences in biological materials, and they should be used regularly in IVF laboratories. In addition, EWSs can be actively used in genetic laboratories during the IVF process and biochemistry laboratories.

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METABOLIC ENDOTOXEMIA AND MALE INFERTILITY

Infertility is a global health problem affecting 10–15% of couples in reproductive age. There is growing evidence supporting that lifestyle factors can affect male fertility through alterations in endocrine profiles, spermatogenesis and sperm function. Thus, the identification of the factors contributing to infertility may be critical to offer simpler and/or more effective therapeutic options than the general spectrum of available treatments. The increasing worldwide prevalence of metabolic syndrome (MetS), especially in younger populations, is a risk factor for fertility disorders. However, a direct correlation of MetS with male infertility still remains unclear. Obesity and a diet high in fat or calories that is typically consumed by obese individuals, has been reported to cause a breakdown in the normal gut mucosal barrier function, leading to the passage of gut bacteria membrane remnants into the systemic circulation, initiating a chronic state of systemic inflammation. Inflammation, particularly in adipose tissue, has been implicated in diet and obesity related insulin resistance in experimental models [1].

Gómez-Elías er al [2] induce a metabolic syndrome like condition in experimental model. (C57BL/6xBALB/c) F1 male mice were fed a high-fat diet (HFD, 30% fat) for 19 weeks, while controls received a normal-fat diet (NFD, 6% fat). HFD-fed animals exhibited increased body weight, hypercholesterolemia, hyperglycemia and glucose intolerance. HFD-fed males exhibited a higher amount of gonadal fat, proposed to increase testicular and epididymal temperature, thus

affecting sperm production, maturation and storage. However, HFD-fed mice exhibited a decrease in epididymal weight, consistent with the lower epididymal sperm count. Also, sperm analysis showed significant differences between HFD- and NFD-fed mice in cauda epididymal sperm count, sperm viability, morphology and progressive motility. Ning Ding et al [3] investigate if HFD-induced gut microbiota dysbiosis can functionally influence spermatogenesis and sperm motility. Feacal microbes derived from the HFD-fed or normal diet (ND)-fed male mice were transplanted to the mice maintained on ND. The gut microbes, sperm count and motility were analysed. Transplantation of the HFD gut microbes into the ND-maintained (HFD-FMT) mice resulted in a significant decrease in spermatogenesis and sperm motility, whereas similar transplantation with the microbes from the ND-fed mice failed to do so. Transplantation with HFD microbes also led to intestinal infiltration of T cells and macrophages as well as a significant increase of pro-inflammatory cytokines in the epididymis, suggesting that epididymal inflammation have likely contributed to the impairment of sperm motility. RNA-sequencing revealed significant reduction in the expression of those genes involved in gamete meiosis and testicular mitochondrial functions in the HFD-FMT mice. Ning Ding and co-authors revealed an intimate linkage between HFD-induced microbiota dysbiosis and defect in spermatogenesis with elevated endotoxin, dysregulation of testicular gene expression and localised epididymal inflammation as the potential causes [3].

Obesity and a high fat/high calorie diet are both reported to result in changes to gut bacteria and intestinal wall permeability, leading to the passage of bacterial endotoxin (lipopolysaccharide- LPS) from the gut lumen into the circulation (metabolic endotoxemia), where it initiates systemic inflammation. Endotoxin is known to reduce testosterone production by the testis, both by direct inhibition of Leydig cell steroidogenic pathways and indirectly by reducing pituitary LH drive, thereby also leading to a decline in sperm production. Gram negative bacteria, which comprise 70% of the total bacterial load in the human gut, contain a potent immune stimulant in their cell wall referred to as lipopolysaccharide (LPS) or endotoxin. Animal experiments and human observational studies have shown that consumption of diets containing either high fat or high number of calories leads to significant changes in gut bacterial populations and increases in the circulating levels of plasma endotoxin, implying a breakdown in gut mucosal wall integrity and the passage of gram negative bacteria membrane potent immune stimulant into the systemic circulation. Interestingly, the magnitude of this “metabolic endotoxaemia” is reported to be more pronounced in mice placed on a high fat diet than an isocaloric high carbohydrate diet, suggesting that dietary fat is more efficient in transporting bacterial endotoxin from the gut lumen into the circulation, possibly mediated by transfer of endotoxin across the intestinal wall in lipid laden chylomicrons. Furthermore, a high fat diet is reported to unfavorably alter the gut microbial composition, leading to an increase in intestinal permeability due to disordered tight junction proteins (zonulin, occludin) and a reduction in the colonic mucous barrier. Kelton Tremellen in his study for the first time postulated that in the gut transmucosal passage of bacterial lipopolysaccharide (LPS) from the lumen into the circulation is a key inflammatory trigger underlying male hypogonadism [4]. High-fat diet has a prominent role in increasing oxidative stress and lowering antioxidant effect. There is mounting evidence that obesity has negative repercussions for reproductive physiology in males. Much of this evidence has accumulated from animal studies employing diets high in fat and sugar (“high fat” or “western” diets). While excessive fats and carbohydrates have long

been considered major determinants of diet induced obesity, a growing body of research suggests that the relationships between diet composition and obesity are more complex than originally thought, involving interactions between dietary macronutrients. Elevation of reactive oxygen species (ROS) may have a detrimental effect on sperm quality and hence fertilization potential. This is undoubtedly good advice, given the clear negative impacts of obesity on male reproduction and the strong relationship between diet and obesity risk. However, there is no clear definition of what a "healthy diet" for reproduction is. Switching to a "healthy diet" for most men means reducing intakes of foods containing saturated fat and added salt and sugars, and eating a wider variety of unprocessed foods (as recommended by nutritional dietary guidelines). There is a clear need to further explore how diet impacts male reproductive function in order to develop evidence-based preconception nutritional guidance for men. Linn B. Hakonsen and co-authors in their cohort study observed that the altered androgen profile tended to improve following weight loss and that weight loss may potentially lead to improvement in semen quality [5]. Karma L. Pearce et al. in pilot study of 37 infertile men confirmed a significant positive correlation between body mass index (BMI), increased intestinal permeability (serum zonulin), metabolic endotoxaemia (LBP), sperm DNA oxidative damage (seminal 8-OHdG) and increasing levels of sperm DNA fragmentation. Metabolic endotoxemia was positively correlated with increasing levels of sperm DNA oxidative damage with this relationship remaining significant, even after adjustment for relevant confounders such as age, BMI and days of abstinence. These observations suggest that metabolic endotoxemia and its associated oxidative stress may be a key driver of sperm DNA damage in obese men [6]. A recent study by Dardmeh et al. [7] demonstrated that probiotics could be an alternative solution in eliminating obesity drawbacks on semen quality. The study was done on male mice to investigate the effect of probiotics (Lactobacillus rhamnosus) on sperm kinematic parameters, testicular weight, lipid profiles and reproductive hormones such as follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone. Probiotics have a positive effect on male fertility by either direct or indirect influence. The direct effect improves spermatogenesis and maturation process whereas the indirect effect works out by eliminating the adverse effects of obesity and elevating the total antioxidant capacity. In another study, Amandine Everard et al. [8] demonstrated that prebiotic (oligofructose) treatment restored Akkermansia muciniphila abundance and improved gut barrier/ gut permeability and metabolic parameters. A. muciniphila improved metabolic disorders in diet-induced obese mice, normalized diet-induced metabolic endotoxemia, adiposity, and the adipose tissue marker CD11c. Similarly, A. muciniphila treatment reduced body weight and improved body composition (fat mass/lean mass ratio) without changes in food intake. This study clearly demonstrated the lack of a direct relationship between the abundance of Gram-negative bacteria within the gut and metabolic endotoxemia (i.e., that is caused by serum LPS) because gut colonization by A. muciniphila decreased metabolic endotoxemia arising on an HF diet. One explanation for this counterintuitive result may be that A. muciniphila regulates gut barrier function at different levels. So, according to previous data gut microbiota contribute to gut barrier alterations during obesity and is the reason of metabolic endotoxemia.

A recent study was carried out by Valcarce et al. [9] to evaluate the effect of two selected anti-oxidant probiotic strains (Lactobacillus rhamnosus CECT8361 and Bifidobacterium longum CECT7347) on sperm criteria of asthenozoospermic men. Four parameters were evaluated: sperm motility, sperm viability, DNA fragmentation, and level of ROS. Viability was not affected while the other three tested parameters

demonstrated a significant improvement after probiotic treatment. These findings give an evidence of the importance of using probiotcs to improve fertlity of human males.

Finally the first placebo-controlled study was conducted by Maret and Cavallini [10] and reported a significant augmentaton in testosterone level and sperm quality of infertle men after using a combinaton of prebiotc/probiotc therapy. Data showed a direct impact of prebiotc/probiotc therapy on the functon of pituitary gland in terms of enhancing FSH and LH serum levels.

Since many studies show that prebiotcs and probiotcs are the key regulators of microbiota improvement, then they may have an influental therapeutc impact on the abovementoned disturbances (metabolic endotoxemia) and in this way may open knew avenue in the treatment of idiopathic male infertlity.

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PREVENTION OF HPV RECURRENCE WITH HPV VACCINATION AFTER LASER VAPORIZATION AND CONIZATION IN REPRODUCTIVE AGE PATIENTS WITH HSIL (PRELIMINARY STUDY)

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Background and Aims

Based on our preliminary data we can supposed, that vaccina t on by “Gardasil” a f er laser surgery of intraepithelial lesion may prevent recurrence in pa t ents with HPV. Preven t on of Human Papilloma Virus (HPV) recurrence by “Gardasil” a f er surgical treatment of pa t ents with high grade intraepithelial lesion HSIL-CIN2 and HPV infec t on.

Methods

There were investigated 145 patients with HSIL-CIN 2. (Pap smear, colposcopy, biopsy, immunohistochemistry P16+).

Results

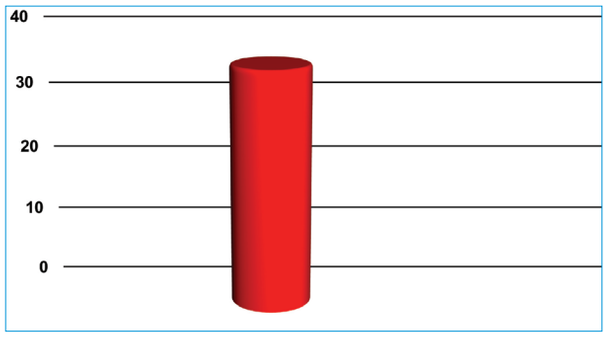
All investigated patients (n=145) with HSIL-CIN 2 were treated by Co2 Laser conization and vaporization. They were suggested vaccination by "Gardasil". Main control group includes 53 patients who agreed vaccination. They were treated by "Gardasil". After surgical procedure and before sexual activity. Study group includes 92 unvaccinated patients. There were made control PAP smear, colposcopy and PCR detection of HPV (Type – 6,11, 16, 18, 31) infection after surgical treatment with 3 months intervals during one year. HPV induced lesion was statistically significant at 6, 9 and 12 months ($p<0.05$).

Conclusions

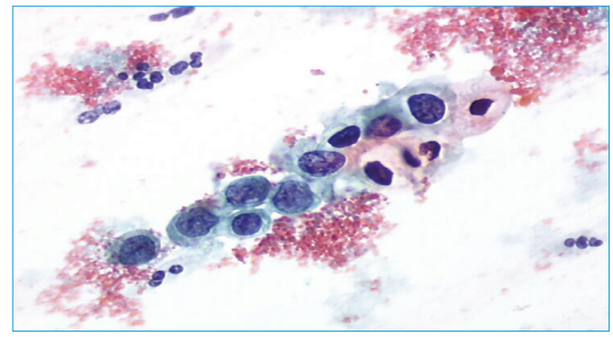
Based on our preliminary data we can supposed, that vaccination by "Gardasil" after laser surgery of intraepithelial lesion may prevent recurrence in patients with HPV.

In study group there was found cases of HPV induced lesion:

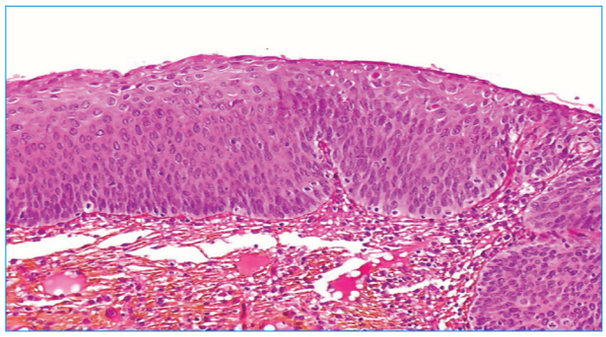
Diagnostic Methods	Study Group Without Vaccination n - 92	Control Group After Vaccination n=53	Time After Conization and Vaporization months
Colposcopy	Adequate, acetowhite epithelium (2.7%)	Normal Colposcopy	3 months
	Adequate, acetowhite epithelium, fat condyloma (5.9%)	Normal Colposcopy	6 months
	Adequate, acetowhite epithelium, fne punctaton (9,7%)	SCJ Visible	9 months
	Adequate, fne punctaton and mosaic (16,7%)	SCJ Visible	12 months
Pap smear	NILM	NILM	3 months
	LSIL - CIN 1 (HPV)	NILM	6 months
	LSIL - CIN 1 (HPV)	Squamous Metaplasia	9 months
	LSIL - CIN 1 (HPV)	Squamous Metaplasia	12 months
PCR	HPV - Negatve	HPV - Negatve	3 months
	HPV - Positve	HPV - Negatve	6 months
	HPV - Positve	HPV - Negatve	9 months
	HPV - Positve	HPV - Negatve	12 months



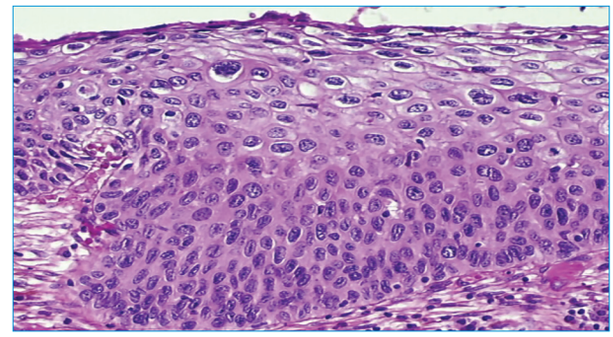
witout Gardasil after Gardasil



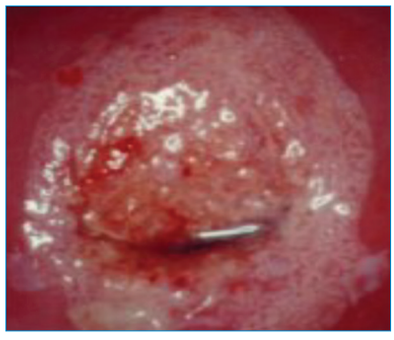
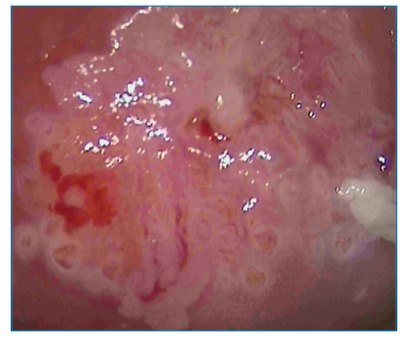
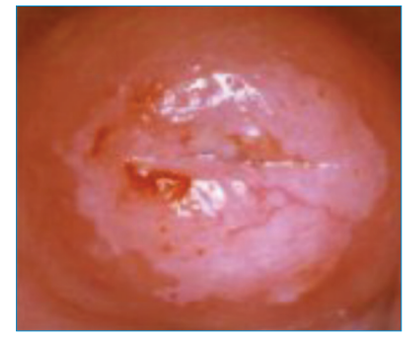
Pap smear HSIL, CIN+



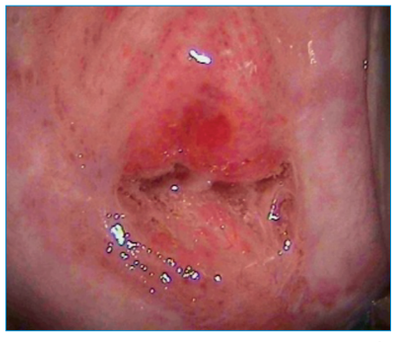
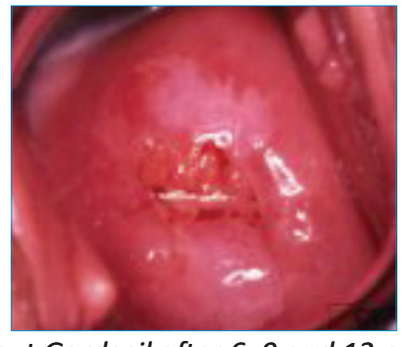
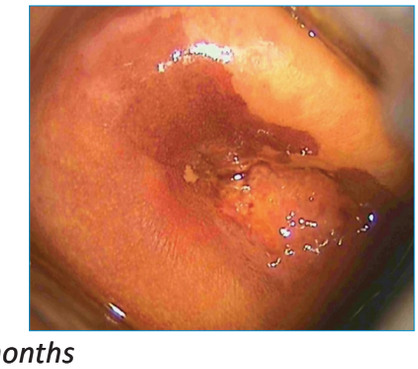
Biopsy, Histology HSIL+



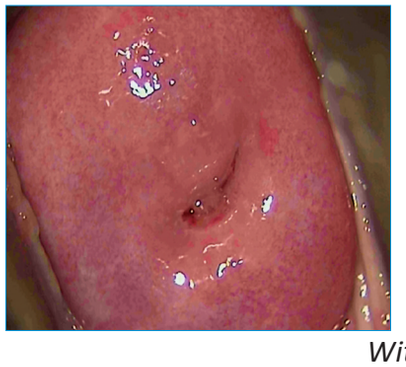
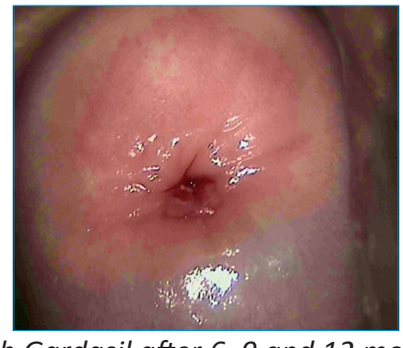
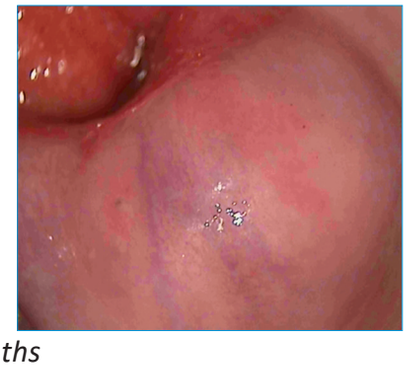
Immunohistochemistry P16+

HSIL Colposcopy

Without Gardasil after 6, 9 and 12 months

With Gardasil after 6, 9 and 12 months

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FERTILITY SPARING IN CERVICAL CANCER

Cervical cancer is the fourth most common cancer among women worldwide and affects women at a significantly younger age than most other malignancies. Approximately 42% of the women diagnosed with cervical cancer is ≤45 years. Combined with a trend towards delayed childbearing, many of these women may desire to preserve their fertility at time of cancer diagnosis.

The aim of this lecture is to give an overview of current fertility-sparing treatment options for invasive cervical cancer.

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PRESERVATION OF FERTILITY IN ONCOLOGICAL PATIENTS OF REPRODUCTIVE AGE

Peace Consensus for a New Discipline of the Future – Oncoreproduction

Malignant neoplasms in patients of reproductive age are an important medical and social issue of modern healthcare in all countries. 2,191,040 new cases of cancer were found in patients under the age of 45 worldwide in 2020, which is 11% of all cases of cancer (Globacan). Advancement of the methods of diagnosis and treatment of oncological diseases results in improvement of the rates of recurrence-free and overall survival of patients, which should be supported by a good quality of life.

For the vast majority of cancer patients of reproductive age, the prospect of delayed childbearing and possibility of having biologically natural children after recovery are extremely important. Any oncological treatment may be associated with gonadotoxic effects of chemotherapy medicines, radiation treatment, surgical castration and requires long-term follow-up. Discussion of issues related to fertility with young patients should definitely be included in counseling before the start of specialized therapy, implying a favorable prognosis of the disease (Lambertini M. et al., 2016). It provides for adherence to treatment and post-oncology rehabilitation.

Based on our experience, consultation on fertility preservation should be carried out in view of a specific treatment strategy for the patient, that is established after assessing the dissemination

of the oncological process by expert histological examination of the tumor, including immunohistochemical examination to identify the significant degree of expression of steroid hormones, to determine the presence of mutations in hereditary forms of cancer. All this makes it possible to form an opinion on the possibility of organ-preserving treatment, the gonadotoxicity of the planned therapy and the prognosis of the disease. Based on the results obtained, a set of individual measures to preserve the reproductive potential and options for achieving pregnancy after recovery can be proposed. Informed patient's decision to preserve fertility should be based on competent informing only.

We managed to develop an interdisciplinary algorithm for organizing timely care for this group of patients and put into practice the principle of quick collegial (oncologist and fertility specialist) decision-making even before or during specialized oncological treatment. Important components of this standard are:

- compliance with time frame between making the preliminary oncological diagnosis and consulting with a fertility specialist – no more than 1-2 days:
- conclusion of the oncological multidisciplinary case conference for each patient in a specialized expert-level institution on choosing a method of reproductive technologies for preservation of biological material of the patient;
- ability of the reproduction clinic to immediately provide the full range of advanced technologies for obtaining and cryopreservation of the biological material, including IVM, OTO-IVM and cryopreservation of ovarian tissue;
- competent and timely provision of legal accompanying information to patients, which is especially important in matters of use of embryos;
- secure transportation of biological material in compliance with all standards, including temperature range and time of delivery of the material to the embryological laboratory;
- training of medical personnel working with oncological patients (clinic administrators, nurses, biologists, laboratory assistants, anesthesiologists, and others).

Since March 2021, after signing a memorandum on professional cooperation with the Next Generation Clinic of Reproduction (Saint Petersburg), more than 400 patients aged 18 to 45 have been consulted about fertility preservation in N.N. Petrov NMRC of Oncology (Saint Petersburg); 85% of them were women and 15% men. Nosological forms of oncological diseases were as follows: 31% of the patients were with malignant tumors of the reproductive system, 26% – with malignant tumors of the mammary glands, 15% – with hemoblastoses, 10.2% – with tumors of bones and soft tissues, 8.7% – with germ cell tumors, 9.1% – patients with tumors of other organs, including brain tumors. The result of close cooperation with the fertility specialists of the Next Generation Clinic (Saint Petersburg) was cryopreservation of the biological material of 107 cancer patients. 65 ovarian stimulations for cryopreservation of oocytes and embryos were carried out as a part of Delayed Motherhood program, taking into account the results of immunohistochemical pathomorphological tests of the tumors, which amounted to 20% of all consulted women. The average age of patients who took advantage of the possibilities of assisted reproductive technology methods was 28.4 years (from 19 to 42 years). 7 intra-

operative specimens of the cortical layer of the ovaries were taken for maturation of oocytes of the ovarian tissue outside the body (OTO-IVM). Oocytes of 4 patients were cryopreserved. 3 patients were referred for IVM to the reproductive clinic due to uncertain risks of ovarian stimulation.

Over 40 men with testicular germ cell tumors and hematological malignancies used semen cryopreservation services before starting chemotherapy, which accounted for about 80% of all consulted male patients. The average age was 28.4 years.

More than 40 patients were consulted in connection with the expiration of the follow-up period on safety issues and methods of achieving pregnancy, some of which were referred by obstetricians-gynecologists for the prolongation of an already ongoing pregnancy. 26.7% of all consulted patients took advantage of the modern possibilities of assisted reproductive technologies (ART) for preservation of biological material, which corresponds to international parameters for the implementation of measures to preserve fertility.

Oncologists should inform patients about the possibilities of organ-preserving treatment and strategies for implementation of fertility, which require a multidisciplinary approach (from oncologists, surgeons, pathologists, reproductive specialists and embryologists). Patients who received full information about the risk of infertility as a result of cancer treatment and about possible measures to preserve reproductive function are significantly less worried about the aggressive treatment and have higher potential for cure. Potential iatrogenic loss of fertility, loss of a potential child, has a profound emotional impact on young women and can sometimes be more stressful than the cancer diagnosis itself (Letourneau J.M. et al., 2012).

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TWENTY-SIX YEAR RESULTS OF THE ISRAELI-GEORGIAN PROGRAM DIABETES IN PREGNANCY

Background

The number of people with diabetes globally reached 537 millions in 2022, since 2019 this number increase by 16%; 90% of all cases are type 2 diabetes. In 2021 Type 2 diabetes was diagnosed in 1 200 000 children and adolescents. It is estimated that 21.1 million (16.7%) of live births to women in 2021 had some form of hyperglycemia in pregnancy. Of these, 80.3% were due to gestational diabetes mellitus, while 10.6% were the result of diabetes detected prior to pregnancy, and 9.1% due to diabetes (including type 1 and type 2) first detected in pregnancy (IDF Atlas, 10-th ed., IDF, 2021). Proper treatment and use of high quality insulin plays the pivotal role in the management of diabetes in pregnancy. For several decades people with diabetes and mainly pregnant women with diabetes are using high quality insulin preparations (Novo Nordisk and Sanoif). The Israeli-Georgian Program Diabetes in Pregnancy was initiated at the Georgian Diabetes Center (now National Center for Diabetes Research) in 1996, with the aim to provide care for women with diabetes. The Program has become possible as a result of Twinning between Georgian Union of Diabetes and Endocrine Association and Israeli Diabetes Association.

The aim of the present work to assess the e f cacy of treatment in women with Preexist ng Diabetes (T1DM) and GDM. Clinical data of the study popula t on:

Materials and Methods

Totally, 407 Women with Preexis t ng Diabetes/T1DM and 119 Women with GDM were enrolled in the study. They were divided into 4 groups (Gr): Gr.1 – 223 pa t ents who received pre-concep- t on care; Gr.2 – 118 pa t ents enrolled in the program at gesta t on age < 10 weeks ; Gr.3 – 66 pa- t ents enrolled in the program at gesta t on age > 10 (11 – 21) weeks and Gr.4 – 119 pa t ents with GDM.

	Gr.1 (N=223)	Gr.2 (N=118)	Gr.3 (N=66)	Gr.4 (N=119)
Age (years)	22.9 ± 4.6	23.5 ± 5.1	23.2 ± 4.1	25.9 ± 5.3
Diabetes duration (years)	10.9 ± 7.2	11.7± 6.4	9.8 ± 6.9	-
Preconception care	Yes	no	no	no
Pre-pregnancy BMI (kg/m2)	21.6 ± 3.6	22.4 ± 2.4	23.3 ± 1.9	24.8 ± 4.9
HbA1c (%) before treatment	8.12 ± 0.5	8.17 ± 0.6	8.09 ± 1.6	6.7 ± 0.9
Preproliferative retinopathy (%)	8.96	13.5	13.63	-
Microalbuminuria (%)	6.27	11.86	16.6	10.08

All women were followed-up throughout preconcep t on care and pregnancies. Following pa- rameters were controlled: 1) BG: fas t ng – 60-90 mg/dl, postprandial 1-hr < 140mg/dl, postpran- dial 2-hr < 120mg/dl, before meal – 75-105 mg/dl; HbA1c < 6.5 %; Correc t on of intensive insulin therapy based on the SBGM; Avoid of sever hypoglycemia episodes. 2) Blood pressure control. 3) Ultrasound examina t on, cardio monitoring of a fetus. 4) Obstetrical/ gynecologic follow-up. 5) Folic acid supplement (5 mg/d). Strict metabolic control was achieved during preconcep t on care and maintained throughout pregnancies. Screening for GDM revealed the condi t on in 119 pregnant women (75-g OGTT was performed at 24-28 weeks of gesta t on).

Results

At entry HbA1c(%) levels for Gr.1, 2, 3 and Gr.4 were: 8.12 (0.05), 9.08 (0.6), 8.09 (1.6), 6.7(0.9) respec t vely; By the end of preconce t on care HbA1c levels in Gr.1 – 6.0(0.65)% were sta t s t cal- ly lower in Gr.2 and 3 (P=0.000). By term HbA1c levels sta t s t cally decreased in all the groups (P=0.024, P=0.000, P=0.000, respec t vely). The rate of spontaneous abor t ons was lower in Gr.1 (2.24%), than in Gr.2 (8.4%) P=0.000. In Gr.1 pa t ents percent of pre-eclampsia (0.44%) was lower, than in Gr.2(8.4%) and Gr.3 (10.6%) (P1-2 =0.0005; P1-3 = 0.0002). No sta t s t cal di f erence be- tween Gr.1 and Gr.4 was revealed. In Gr.1 pa t ents percent of preterm deliveries was lower, than in Gr.2 and Gr.3 (P1-2 =0.0014; P1-3 = 0.0001). No sta t s t cal di f erence between Gr.1 and Gr.4 was revealed. In Gr.1 pa t ents percent of macrosomia was lower, than in Gr.2 and Gr.3 (P1-2 =0.0074; P1-3 = 0.0101); and in Gr. 1 and 4 (10.47 – 11.7%) – no sta t s t cal di f erence was observed. Perina-

tal mortality was observed in Gr.1 – 1.79%, in Gr.2 – 4.23% in Gr.3 – 7.5% and in Gr.4 -1.68% (P1-2 =0.0944; P1-3 = 0.0129; P1-4 =0.7265).

Clinical Data in Women with Preexisting diabetes mellitus and gestational diabetes mellitus.

	Gr.1= 223	Gr.2= 118	Gr.3= 66	Gr.4=119 GDM
Preeclampsia	1 (0.44%)	8 (6.7%)	7 (10.6%)	1 (0.84%)
No of deliveries Vaginal (%) Cesarean section (%)	 40.9 52.9	 31.4 64.4	 23.7 77.2	 49.6 48.7
Gestational weeks of delivery	36 - 40	35 - 39	32 - 39	35 - 39
Preterm delivery <37 weeks	10 (4.8%)	14 (11.8%)	9 (13.6%)	8 (6.7%)
Preterm delivery <34 weeks	-	2 (1.6%)	6 (9.9%)	3 (2.5%)
Birth weight (g)	3655±505.4	3469 ±491.1	3487±642.3	3495 ± 493.5
Spontaneous abortions (%)	1.7	7.62	-	-

Clinical Data in 232 Women with Preexisting diabetes mellitus and 71 Women with gestational diabetes mellitus.

	Gr.1= 223	Gr.2= 118	Gr.3= 66	Gr.4=119 GDM
Macrosomia	59 (26.4%)	33 (27.9%)	19 (28.7%)	29 (24.3%)
Neonatal hypoglycemia	12 (5.3%)	15 (12.7%)	10 (15.1%)	12 (10.08%)
Respiratory distress syndrome	3 (1.7%)	6 (5.08%)	8 (12.1%)	5 (4.2%)
Major congenital malformations	-	-	3 (4.5%)	1 (0.8%)
Stillbirths	3 (1.34%)	3 (2.54%)	6 (9.9%)	1 (0.84%)
Neonatal death	0	2 (1.69%)	2 (3.03%)	1 (0.84%)
Perinatal mortality per 1000 births	13.4	42.3	-	-

Conclusion: 1) If in patients with Preexisting DM diabetes control was achieved before conception, risk of spontaneus abortons, was significantly lower, than in patients, in whom treatment was initated already after conception. 2) In patients with Preexisting Diabetes and GDM good glycemia control during pregnancy significantly reduces the risk of pre-eclampsia, preterm delivery, and perinatal deaths. 3) This program shows that proper approach to pregnancy management in diabetes can be successfully implemented even in low-to-middle income countries.

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INCIDENTS AND MISTAKES IN IVF

The era of in vitro fertlizaton (IVF), as part of medicine had been started when Louise Joy Brown came to being due to IVF procedure atempt on July 25, 1978. Robert Edwards and Patrick Steptoe were the frst pioneers in IVF who successes this new feld in medicine and open the source for the development of a new subject – clinical embryology.

Twenty years later, in 1998, the sensatonal news was reported in the front-page artcle: "A black-skinned child was born by white woman". Yah, curiously weren't mistakes in IVF during these twenty years or maybe the unnotced errors? Likelihood, the misconducts in IVF weren't exposed to public. A year later, in 1999, a white woman from New York gave birth for twins-boys: white and black. This woman had been treated in one of IVF clinic in Manhatan and had been undergoing the embryo transfer simultaneously with a black woman. Coincidently, an embryo from the black woman ended up into the white woman, most likely due to improperly fushed catheter. In the issue, only the white woman became pregnant.

The same incidence was occurred on July, 2002 in UK. A white woman was delivered black twins due to mix-up in NHS fertlity clinic. This IVF's careless, thought to be the frst, which was revealed in UK. The possible reason of this uncommon situaton could be a fertlizaton of white woman's egg by black man spermatozoa. Moreover, now the ethic issue is raising up who are the real parents of the twins?

In 2004, a Californian woman had compensaton in 1 million dollar because she was transferred by wrong embryo in IVF clinic and this mistake was revealed 10 months later afer delivery of a baby.

In 2007, IVF clinic in Cardiff (UK), thawed embryo that belonged to 42 years old lady was incidentally transferred to another woman. Cardiff IVF clinic admitted liability and paid the couple an undisclosed sum of money, reportedly about 25,000 £. In 2009, in Israeli Porya IVF clinic, a woman had been implanted with thawed embryos, belonged to another couple due to mix-up. The same case in the same year was reported in Ohio, USA. Despite of this misstep, the couple has been decided to continue with this pregnancy. Right after delivery the newborn gained his biological parents.

The errors in IVF could be easily revealed by the different skin color or physical features of newborns. However, in the absence of evidence the IVF's careless is difficult to discover. The misconducts in IVF procedures are quite rare, but definitely could happen in any IVF clinic around the world. Can they really be prevented? Human errors are very difficult to prevent, but they could be predictable. It is needed to be understood what are the reasons of human errors in IVF (as also in other professions). The possible reasons could be fatigue, workload, variability in messages perceptions loading to behavioral impact, poor interpersonal communication, invalid supervision, and team work issues.

Fatigue can be triggered by sleepless, preoccupation, multitasks, oxygen less in the workplace, and stress. Workload can be induced by overload in the workplace, multitasks, and stress. Variability in message perception could be individually based or based on gender dependent structural and functional differences in the human brain. Interestingly to note, the male brain shows hemispheric asymmetry: the left hemisphere functionally looks different from the right hemisphere. Indeed, the two hemispheres of female's brain are much more alike. In women, there is proportionately more grey matter, and less white matter; vice versa for men. It has been shown that women and men have different perception for messages. They listen, read and express emotions in a different ways. The causative reason of this difference is that men are most likely use a less capacity of their brain than woman who uses both hemispheres for the same task. The different perception loads to different social behavior, which could lead to poor interpersonal communication, misguidance, and ability to make the right decision. It was shown that brain is rational, but not very objective. For these reasons, artificial intelligence (AI) that does not depend on our perception of incoming information, would help good judgment and make correct conclusions and better decisions.

Another major subject of missteps could be distracting conversations in the working place including the phone talks, which can divert the attention of workers from their tasks. "Coffee blah, blah, blah" is keeping worker's attention away from their job thereby increasing risks of errors.

To prevent the oversights it is very important to keep "positive" work environment in workplace, which means trust, cooperation, safety and risk-taking support. There must be a common understanding and cohesion in the working team. The toxic atmosphere may occur when there are no support for workers from management, no support between the workers themselves, lethargy, absenteeism, verbal and physical intimidation, increased levels of complaints, changes in employee's behavior, a pervasive culture of fear.

In last, in order to increase the quality of IVF laboratory and to eliminate the likelihood of failure it is important to standardize the methodology and the working processes. For this purpose, it is necessary to arm the standard operation procedures (SOPs), quality control, to provide the periodically training of employees and to conduct the annual audit and inspections.

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MENSTRUAL DYSFUNCTION 35+. A NEW VISION, A NEW TAXONOMY

Menstrual function is a manifest proof of a woman's reproductive health, with certain age-phase bases and features, at the stages of its formation, progress, and involution. The regulation of this important function is quite complex at the hypothalamic-pituitary-ovarian level.The long-standing nomenclature/taxonomy implemented in clinical practice has changed over the last 5 years to a patient/woman and quality of life orientation. Updates in this regard concern both diagnostic methods and clinical management practices, surgical and conservative (drug) management.

Special emphasis is placed on the disorders and management features of the puberty period depending on the seriousness of the age stage. Management of late reproductive age (progesterone-deficient period), pre-, peri- and menopausal dysfunction is also very important, especially in the category of reproductive planning.

For the management of menstrual dysfunction in late reproductive age, it is important to take into account the physiological, metabolic and somatic features of age. The work highlights the special properties of progestagen – dydrogesterone; Peculiarities of management of menstrual dysfunction; The main characteristics of dydrogesterone – powerful progestogenic activity, without antigonadotropic, mineralocorticoid/antimineralocorticoid, estogenic, androgenic/antiandrogenic activites; not metabolized to estrone; does not affect the synthesis and metabolism of endogenous progesterone; Does not affect ovulation; It is also possible during metabolic prob-

lems and hypertension; oral and easily acceptable comfortable form; Has a pronounced ability to affect embryoprotective gravidarum immunomodulation.

The paper focuses on recent works that highlight the role of dydrogesterone in the treatment of excessive/intentional menstruation [8], various effective regimens in the treatment of dysmenorrhea [9, 10, 12,13,14,15,16]. The benign profile of dydrogesterone and the practice of safe use in combination with other medications have been described [11]. Its role is especially important in pre- and post-menopause [17].

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IMPORTANCE OF EXPANDED CARRIER SCREENING AMONG OOCYTE DONORS – QUESTIONS AND CONCERNS

Study question

To examine the utility of a range of expanded screening panels for oocyte donors.

Summary answer

Expanded carrier screening with NGS data identified that 86% of gamete donors were carriers of at least one condition while 302 genes were tested.What is known already: The level of genetic testing for oocyte donors is not regulated in most countries. The use of expanded carrier screening is recommended more widely. If the egg donor is a carrier, there is a 50% chance that the offspring will also be carriers. Expanded carrier screening is performed to determine the potential effects of positive carrier status, which guarantees safety for future pregnancy. From practical experience, more genes are tested for a donor, more potential mutations are detected.

Study design, size, duration

A cohort of 92 potential oocyte donor applicants aged 18-30 years old, who were qualified for oocyte donation after full screening, tested negative on an initial cystic fibrosis carrier test for 11

most common CFTR mutations (PCR panel), was further screened with expanded commercial carrier testing panel (302 genes) using next-generation sequencing (NGS) data. Participants/materials, setting, methods:A cohort of 92 potential oocyte donor applicants aged 18-30 years old, who tested negative on an initial cystic fibrosis carrier test for 11 most common CFTR mutations (PCR panel), was further screened with expanded commercial carrier testing panel (302 genes) using next-generation sequencing (NGS) data. Main results and the role of chance: Genotyping results for all donors were analyzed; 38% (35/92) of donors were identified as carriers for one condition, 34% (31/92)- for two conditions, 7% (6/92) – for three conditions and 7% (6/92) – for four conditions, including cystic fibrosis. Among the most prevalent conditions in our study were: Hemochromatosis: Type 1: HFE Related – 22%, Cystic Fibrosis: CFTR-related conditions 11%, Biotinidase deficiency – 7,6%, 21-Hydroxilase-Deficient Congenital Nonclassical Adrenal Hyperplasia – 6,5%, Krabbe disease – 6,5%, Usher syndrome: USH2A-related conditions – 6,5%, Nonsyndromic deafness: GJB2- related conditions – 5,4% and Smith-Lemli-Opitz syndrome (5,4%).

Limitations, reasons for caution

Each donor was consented for genetic testing.

Wider implications of the findings

This study shows a need to provide the explicit requirement for oocyte donor genetic testing and guidelines to satisfy quality and safety and not reduce the number of donors carries of mutations, but to implement a practice of genetic matching.

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GLOBAL NEED IN OOCYTE DONATION - EGG BANKING

Third-party reproduction has become one of the widely used fertility treatments that involve use of gametes or embryos. With the improvements in oocyte cryopreservation techniques, a new era of health tourism has been initiated. The first oocyte donation was performed in 1983 in Austria and since then it has become a part of routine assisted reproductive technology (ART) treatments. Thousands of oocyte donations have been applied throughout the world resulting in thousands of births. The main drive of oocyte donations is the inability of females to get pregnant using their own gametes due to poor oocyte quality after several failed in vitro fertilisation (IVF) attempts or low/absent ovarian reserve because of advanced maternal age or premature ovarian failure. Oo-cyte donation can also be offered to woman with a heritable genetic disease to prevent the transmission of the disorder to the next generation, though preimplantation genetic diagnosis is usually preferred with no history of infertility. Least commonly, oocyte donations can be offered to same-sex male couples in adjunct to surrogacy.

Egg banks are developing widely in the World and offering different services, however not all of them are similar and there some critical points health care professionals and patients should pay attention while selecting an oocyte bank:

1. The first of all, any egg bank must have a registration of the legal entity! Now many of agencies or companies which consider themselves as an egg bank are not a legal entity,

and they can't use biological material for trading purposes. Also, they can't take responsibility for biological material storage and distribution. Most of egg banks just present a good-looking website and nothing more. These kinds of companies or agencies do not take any responsibility, but they shift the responsibility to medical clinics. When a clinic places an or-der from such an egg bank, they surprisingly find out they need to make a payment not to the egg bank but to the supplier clinic.

The main risk is you won't be given any support or assistance in case of any difficulties. When you will try to reach them, they will show the address of the clinic since they do not holder themselves accountable because they are a non-legal entity "Egg Bank". Their defense will be – they were promoting trademark of the supplier clinic.

2. Secondly, A legal entity of an egg bank must have a medical director, a scientific director, and a lab director. This is the main criteria you can trust as a legal entity of an egg bank. Many banks mention they are under supervision of a well-known star! Also, they are ad-vertised that big-name scientific advisors or consultants work for them. However, this is only a marketing trick. Because those people are not official employees in that egg bank and they do not have any in-house physical presence. These people do not perform daily routine work, or they do not take any responsibility for biological material creation, storage, or distribution. You must know about education, experience, and leadership capability of medical director in an egg bank. The same criterion is applied for a lab director. A Lab director must have extensive and considerable experience in cryopreservation, storage, and movement of biomaterial. Many egg banks just hire several doctors and an embryologist meanwhile they position themselves as a legal entity of egg bank. All other employers work either part time or remotely.
3. Thirdly, the equipment of an egg bank is essentially important. According to the recommendations of ESHRE and ASRM quality of equipment may affect the result up to 70%. The equipment quality, a lab team who uses the equipment and the laboratory environment are 3 key and influencing factors according to ESHRE and ASRM recommendations.

If you try to create a high standard of egg bank you need to have excellent and high quality laboratory. All equipment must have CE mark and annual service reports as well as operations. While all of us use cell phones and we understand that over the time cell phones are updated and getting much better and more useful. The same thing we need to consider for IVF equipment. After long time of usage, IVF equipment will start to lose function and will become old in terms of the quality standards. Now equipment is being improved every year especially in the reproductive medicine. Equipment quality will change the outcome even if you use low quality of sperm, egg, or embryo time to time.

4. One more aspect to pay attention to is traceability, aka double witnessing or electronic witnessing. Most of the clinics don't consider investing in electronic witnessing or to employ

one more embryologist for a double witnessing. If a clinic uses regular IVF cycles, situaton is simple unlike with a double control and signature of both embryologists. But when an actve egg bank does up to 100-eggs pick ups per month and which has a storage of up to 10.000 of eggs making double witnessing becomes very risky and limited. If an egg bank or a clinic don't have RFID electronic witness system or any computer sofware for tracking there will be always a risk of mixed up biological material. For a clinic or an egg bank that do not use double witnessing or electronic one there will not be a possibility to fnd a mistake or a proof of the mistake witnessing in case of mixed up biological material.

5. Additonally, the document fow, donor database control and arrangement, storage of documentaton and editng right of the documentaton are important processes for egg banking. Most of the egg banks work with simple Excel or Google sheets which are very limited and difcult to control algorithm. Those systems are not trackable and may allow anyone to make basic changes regarding donor informaton and donor medical card. Unfortunately nobody will easily notce any changes in case of a mistake. Especially in case of extra ordinary situatons, if a baby were born with genetc anomaly, controlling the material in the past and a documentaton system will be impossible.
6. Reimbursement is another critcal factor. Many egg banks state they produce high quality biomaterial. If an egg banks provide a guarantee and a compensaton system under ESHRE criteria (as survival rate, fertlizaton, and blastocyst rate) that means this egg bank is following a strict algorithm. Mostly such egg banks even give much higher percentage of survival rate or blastocyst rate than all statstcs which are published.
7. Lets look at another important factor, it is a country and storage of the material. Mostly, partners understand that today most banks operate in the post-Soviet market, and therefore, there are the risks of a falsifcaton and non-compliance of the chosen donor's biological material, as well as the risk of not being able to sue the bank. The corruption in the post-Soviet countries is a serious issue. And when you choose a bank located in a post-Soviet country, you must clearly understand and assess all these risks that could seriously afect your future reputaton and the inability to receive any compensaton or a court decision, or on the other hand experience the birth of a child with genetc defects and pathologies. Therefore, the locaton of a bank should be carefully noted!

Or, if you have decided to use a bank in that locaton, the biological material must comply with pre-determined and strict criteria. Many major world banks buy biological materials in the post-Soviet countries, but accordinly the risk then falls on these bigger banks, and you don't have to worry because the latest bank is responsible for its own reputaton.

8. Besides, Customer care is a noteworthy process of an egg bank. High quality egg bank will always fallow such rules:
   - Customer should get a response within 24 hours
   - Customer should get access to a catalogue within 24 hours

- Customer should receive a contract within 24 hours
- Customer needs to get medical informaton within 24 hours
- Customer needs to get communicaton with team and chief embryologist
- Customer needs to get communicaton with the chief doctor within 24 hours

9. On the top of all that, Safety and Ethics are essental to an egg banks. Especially recruitment of egg donors, their compensatons, medical preparaton of egg donors and their standards should be within moral ethics and legal considerations. Egg Banks must adhere safety and quality stmulaton protocols with high quality hormonal medicatons, number of stmulatons as well as breaks between stmulatons
10. Finally, New Technologies in IVF Laboratory: The new way of biological material quality control and selecton has been developed and became much more computer based. Many parts of diferent processes in medical area are controlled and processed by artfcial intelligence. Human eyes are limited especially under a microscope. The future is for Artfcial Intelligence since it gives us sheer perfecton in a morphology base. The System can keep simultaneously tracking a sample, a supplier, an embryologist, and the quality of material which are priceless for a high-quality egg bank. Electronic storage mapping system is another promising technology which allows you to track automatcally a locaton and an amount of biological material in a storage by the computer system. This provides a high quality of traceability and control mechanism for egg banks.

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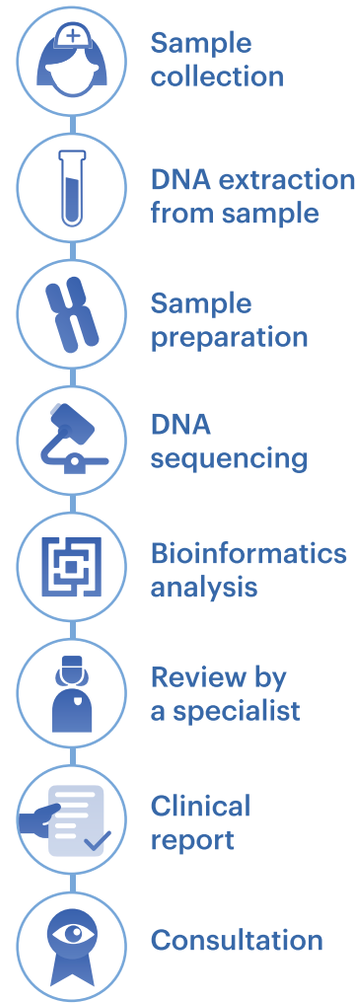
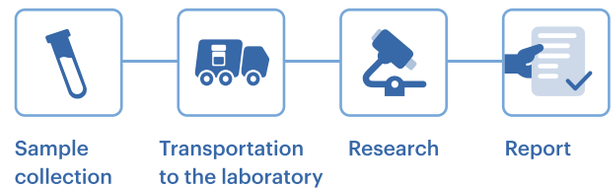
Kromos is the first genetics laboratory of Georgia, based in Tbilisi, performing a full cycle of all tests for reproductive health, rare disorders, and oncology. We provide medical diagnostic services, using such innovative technologies as **Next Generation Sequencing (NGS)**, **Sanger Sequencing** and **fragment analysis**. These technologies are widespreaded throughout the world in reproductive health, oncology and rare disease diagnostics.

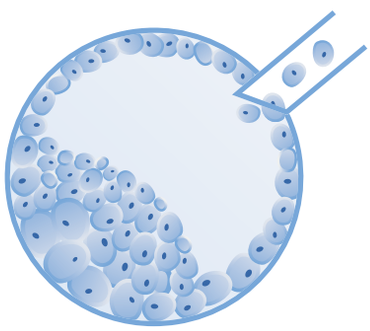
Our mission is to improve people's life quality with the help of high-tech genetic solutions.

Our main goal is the implementation of modern diagnostic solutions in the Georgian healthcare system. The laboratory is equipped with modern technologies in accordance with standards. The team consists of professional geneticists, molecular biologists, bioinformaticians, IT developers who design genetic solutions and perform genetic tests for clinics and patients. This is a step towards the prevention of diseases, diagnosis and selection of adequate therapy, as well as, in general, improvement of the health condition of the population. Knowledge of genetic information and its use for medical purposes can improve the quality and duration of life.



Kromos genetics laboratory can perform diagnostic tests on site without sending all samples abroad, that's why we can provide more advantages in price and time frames without loss of test quality.





In reproductive health, using **Next Generation Sequencing (NGS)** technology, Kromos performs **Preimplantation Genetic Testing (PGT-A)** of embryos for chromosomal abnormalities (aneuploidy). This testing is used during in vitro fertilization (IVF) to detect extra/insufficient chromosomes or their parts in the embryo. PGT-A is a powerful tool for a doctor-embryologist and a patient that helps to make an appropriate decision about transfer of a specific embryo.

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ELECTROMYOGRAPHIC EVALUATION OF THE PELVIC MUSCLES ACTIVITY AFTER HIGH-INTENSITY FOCUSED ELECTROMAGNETIC PROCEDURE AND ELECTRICAL STIMULATION IN WOMEN WITH PELVIC FLOOR DYSFUNCTION

Abstract

Introduction: Impaired coordination, relaxation, and atrophy of pelvic floor muscles (PFMs) may cause various health issues referred to as pelvic floor dysfunction (PFD). In recent years, electromagnetic noninvasive stimulation of the pelvic floor was successfully used to treat PFD symptoms.

Aim: This study aims to compare the effectiveness of electrical and magnetic noninvasive stimulation for the treatment of PFD in postpartum women.

Methods: 2 intervention groups treated with high-intensity focused electromagnetic ([HIFEM]; G1) procedure and electrical stimulation (G2) were established along with the control group (G3). Patients received 10 therapies delivered at the hospital (G1; 2e3 times per week) or self-administered at home (G2; every other day) after initial training. The protocol was identical for both modalities. Functionality of the PFM was examined by surface electromyography measurements (maximal voluntary contraction [MVC]; mean MVC; muscle activity at rest;

endurance of contraction) while patient's subjective perception of pelvic floor functionality was assessed by Pelvic Floor Impact QuestionnaireeShort Form 7 (PFIQ-7) standardized questionnaire. Changes in electromyography values and PFIQ-7 scores were statistically evaluated from baseline to after all treatments.

Main Outcome Measure: The main outcome measure was enhancement of PFM activity.

Results: In total, 95 patients (G1¼50; G2¼25; G3¼20) participated in the study. The MVC, mean MVC, and endurance were lowered in symptomatic patients. After the treatments, these parameters significantly increased (P < .001) and moved toward the values of healthy population. Electrogenesis at relaxation revealed divergent tendencies in the G1 and G2 groups. PFIQ-7 scores significantly improved in treated patients (P < .001). In general, superior results were documented in the HIFEM group as it reached improvement of electromyography parameters from 48% to 59% (electrical stimulation from 7% to 36%) and similarly the improvement of PFIQ-7 score by 57% (electrical stimulation by 32%).

Conclusion: This study documented that the HIFEM procedure was significantly more effective than electrical stimulation in treatment of PFD in postpartum women. Both the objective and subjective evaluation indicates more profound effects of magnetic stimulation. Elena S., Dragana Z., Ramina S., et al. Electromyographic Evaluation of the Pelvic Muscles Activity After High-Intensity Focused Electromagnetic Procedure and Electrical Stimulation in Women With Pelvic Floor Dysfunction. Sex Med 2020;XX:XXXeXXX.

Key Words: Electrical Stimulation; Electromyography; HIFEM Procedure; Pelvic Floor Dysfunction; Pelvic Floor Muscles.

Introduction

Electromyography (EMG) is a method frequently used for examination of electrical activity of muscle tissue. Although this technology is relatively new, it is assumed to be reliable and objective, while causing minimal or no discomfort to patients. Essentially, EMG uses the surface or intramuscular electrodes to record the intensity of signals which propagate in the muscle fibers during the contraction because muscle tissue conducts electrical potentials similar to the nerves. Results of the measurements are expressed as a function of voltage over the time. Except single-fiber EMG,[1] measured values represent a sum of all signals originated from the muscle tissue of certain body area.[2e4]

Besides ultrasound,[5,6] magnetic resonance,[7] manometers,[8] dynamometers,[9] or simple palpation combined with observation,[10] surface EMG (sEMG) is one of the possible objective methods for monitoring resting level, strength, and endurance of the pelvic floor muscles (PFMs). The pelvic floor consists of 3 main compartments – anterior (bladder and urethra), middle (vagina and uterus), and posterior (rectum). Furthermore, there are morphologically complex multilayers of anatomical structures such as pelvic diaphragm (composed of levator ani and coccygeus muscles),

urogenital diaphragm (composed of connective tissue, perineum, bulbospongiosus, and ischiocavernosus muscles), and urethral/anal sphincters. All of these tissues are arranged in the pelvic area and have multiple attachments to the surrounding structures.[11] Under normal circumstances, the PFM prevents multiple disorders such as incontinence (urinary/fecal), sexual dysfunction, or pelvic organ prolapse accompanied with pain and discomfort. However, the atrophy and relaxation of PFMs may promote manifestation of these heath issues, collectively referred as pelvic floor dysfunction (PFD),[10e12] occurring naturally with aging or as a consequence of childbirth.

Recording of sEMG in women who showed certain symptoms of PFD was reported previously by multiple authors. It has been found that EMG is a suitable method for investigation of PFM functioning among healthy subjects and women with signs of urinary incontinence or PFM weakness.[13e21] Despite the various protocols and electrode configurations used, in general, there is a clear relationship between the characteristics of the EMG signal and PFD. In comparison with the healthy and asymptomatic subjects, postmenopausal and even premenopausal women affected by some form of PFM impairment, show distinctively lower EMG values. The intensity of maximum voluntary contraction (MVC) is reduced because the PFMs are weakened and endurance of contraction and muscle activity during rest are affected as well.[13,14,18e20] Aside from sEMG, various subjective questionnaires (Pelvic Floor Disability Index, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire, Pelvic Floor Impact Questionnaire, International Consultation on Incontinence Questionnaire Vaginal Symptoms or Pelvic Floor Bother Questionnaire) were also used to document strengthening and reeducation of the PFM which helped patients to improve their symptoms.[22,23]

Besides the regular exercise,[24] the function of the weakened PFM can be enhanced by noninvasive PFM stimulation. Along with well-established electrical stimulation,[25,26] high-intensity focused electromagnetic (HIFEM) technology is being more frequently used in recent years.[27e29] Both technologies deliver electric currents into the pelvic floor to depolarize membranes of motoneurons to elicit action potential and achieve brainindependent muscle contractions when the action potential of sufficient strength reaches the neuromuscular junction.[30] However, despite the direct flow of electric charge through electrode-tissue surface, the HIFEM induces electrical currents selectively in the PFM by mechanism of electromagnetic induction.[31] As magnetic field passes any medium without attenuation of the energy, the induced contractions may be achieved at greater depths and intensities[32] to possibly provide better outcomes.

Based on the rationale mentioned previously, the aim of this study is to investigate and compare treatment outcomes of the HIFEM procedure and electrical stimulation in women suffering from PFD. The expected changes in PFM activity would be examined by subjective (questionnaire) and objective (sEMG) methods. The measured values will be compared with asymptomatic subjects.

Materials and Methods

Patient's Recruitment Criteria

The inclusion criteria were specified as follows: women of age 18e45 years, who had vaginal delivery, and who already stopped lactation. There were 3 patient groups. The symptomatic patients who reported PFD symptoms related to weakened PFM as lower urinary tract or bowel

symptoms (incontinence) and/or sexual dysfunction (dyspareunia, vaginal laxity, decreased sensitivity during intimacy, inability to achieve orgasm – anorgasmia), were randomly (2:1) divided into the G1 group treated by HIFEM and G2 group which received electrical stimulation. The third group G3 consisted of healthy postpartum patients, to obtain sEMG values of normal population. Exclusion criteria were presence of any metal implants or devices which include metal components, pregnancy, malignant tumor, history of surgical procedure in the pelvic region, presence of pelvic organ prolapse of stage II-IV as per the Pelvic Organ Prolapse Quantification classification, and all general contraindications for physiotherapy. Patients were asked to perform pregnancy test before the first treatment and then retest on a regular basis.

Considerations

This study was approved by the local ethics committee of Hospital Lapino (MD medical group). It complied with ethical principles stated in the Declaration of Helsinki, Convention on Human Rights and Biomedicine, and International Ethical Guidelines for Health-related Research Involving Humans, and it completely excludes impairment of patients' interests and damage to health. All of the subjects were informed about the potential risks and possible benefits of the study, and all participants provided written informed consent.

Treatment Protocol

Both intervention groups received 10 treatments in total addressing the stimulation of PFM. The G1 group was treated using a BTL EMSELLA (BTL Industries Inc, Boston, MA) device, which uses HIFEM technology for noninvasive PFM stimulation and reeducation based on the principle of electromagnetic induction. The device consists of a generator connected to the chair where the stimulation coil is located. The coil emits focused magnetic field of intensities up to 2.5 Tesla, responsible for induction of muscle contraction up to depths of 10 cm. Each therapy with the BTL EMSELLA device lasted 28 minutes, and it was administered under the supervision of a skilled physician at the Lapino Hospital. Patients were seated in a chair, and the intensity of the stimulus was modulated on the scale of 0e100% (0e2.5 Tesla) in accordance with their feedback up to maximum tolerable threshold, when patients felt a strong muscle contraction but without pain or discomfort. All patients have achieved 100% intensity during the first or second procedure. Treatments with HIFEM were addressed 2e3 times per week for a duration of 4 weeks. The sessions were planned to suffice this interval as per the patient/device availability. 2 consecutive treatments were spaced at least 48 hours apart to prevent muscle fatigue.

The G2 group performed home-based and self-administered procedures with a BioBravo (MTRþ Vertriebs, GMBH, Germany) electrical stimulation device. First, the patients were comprehensively trained how to safely and effectively use a BioBravo stimulator. Then, they were instructed to finish treatments at home by repeating therapy every other day. The protocol of stimulation was identical for both groups because the settings of the BioBravo device have been adjusted to reflect those used by the BTL EMSELLA device. Finally, group G3 did not receive any treatment.

sEMG Measurements

The primary outcome of the study was to perform sEMG measurements to determine activation of the PFM in symptomatic and asymptomatic patients and to document the hypothesized changes caused by muscle strengthening. At first, by using a Myomed 632 myofeedback device (Enraf-Nonius B.V., Netherlands), the patients were instructed how to correctly perform contractions of the PFM without (voluntary) involving the muscles of the anterior abdominal wall and gluteal or hip region. When performing contractions, patients were lying in the supine position. During the examination, they were requested to repeat 3 specified PFM activations which consisted of the following: 5 short (quick flick) contractions at maximum intensity with an interval of 10 seconds, followed by sustained contraction and relaxation (both 10 seconds long, 5 repetitions) and finally the sustained contraction held as long as possible to determine PFM endurance.[33]

The sEMG recordings were performed by the Myomed 632 device at the baseline (all groups) and after the patient's last treatment (only G1 and G2). To isolate the signal originated in the PFM, 2 types of superficial electrodes were used: first was applied on the anterior abdominal area (served as reference), and the second (vaginal) electrode was mounted on the intravaginal probe. Neutral gel was always applied on the sensor introduced into the vagina. An experienced physiotherapist confirmed the correct placement of intravaginal probe and PFM contractions. Concurrent registration of muscular electric potential by using the vaginal and skin electrodes allowed differentating PFM contractions. During the sEMG examination, myofeedback (in a form of graph) was displayed on the device's monitor and the external monitor unit which was additionally connected to the device to enlarge the graphic output. The sEMG measurements were performed automatically by the Myomed device, following the pattern of PFM activations described higher. These parameters were acquired for each patient during each visit: MVC, mean MVC, mean activity at rest/resting level (all in mV), and endurance of contraction (in seconds).

Standardized Questionnaire

The secondary outcome was to assess subjective changes in perception of PFD by the PFIQ-7. This standardized questionnaire was used to determine the impact of PFD on the patient's quality of life as it showed to be psychometrically valid and reliable in previous research.[34] Patients from groups G1 and G2 were given the PFIQ-7 at baseline and after the last treatment. Based on their answers, the PFIQ mean scores (on a scale from 0 ¼ no distress to 300 ¼ maximal distress) were calculated and compared against baseline and between the both groups.

Safety

The safety of treatments and sEMG measurements and possible adverse events (AEs) were monitored. Patients were also asked to report any signs of discomfort or pain during the therapies or caused by the positioning of the intravaginal electrode.

Statistical Analysis

All variables were checked for normality by the Kolmogorov Smirnov test. Descriptive statistics were estimated by the sample mean with 95% confidence interval. The differences between groups were tested using analysis of variance test followed by Least Significant Difference post hoc tests. Levene's test of homogeneity of variance was run before analysis of variance to verify the equal variances in groups. Paired variables were tested by a student's t-test. All statistical tests were 2-tailed. Whole statistical analysis was conducted with Statistica v.6 (StatSoft Inc, Tulsa, OK), and the significance level was set as default to 0.05 (5%). Initially, the minimum sample size was verified by using Statistica software. At least 19 subjects must have been included in each of the 3 tested groups, to achieve a power of 80% with a ¼ 5%.

Results

Patient Group Characteristics

In total, 95 patients were recruited during 2018 and early 2019 in accordance with the specified criteria and current state of patients in the clinic: G1 (n¼50), G2 (n¼25), and G3 (n¼20). See Table 1 for detailed characteristics of patient groups. All of the recruited patients from the G1 and G2 groups finished a prescribed number of treatment sessions. 8 patients who reported zero PFIQ7 score at the baseline (G1¼5, G2¼3) were excluded from the questionnaire evaluation. No AEs were observed in regard to the delivered treatments or sEMG measurements. Subjects seldom reported only mild discomfort when recording sEMG using an intravaginal electrode.

Tab. 1. Characteristics of patient groups at the time of recruitment (mean followed by 95% confidence interval)

Group	Age (years)	BMI (kg$m^{-2})	Vaginal deliveries	PFD symptoms (% of patients)
G1 (n ¼ 50)	31.12 (1.52)	23.27 (0.76)	1.76 (0.22)	Urinary incontinence (74%); decreased sexual desire (36%); decreased sensitivity during intimacy (70%); dyspareunia (26%); hypo/anorgasmia (52%)
G2 (n ¼ 25)	31.96 (3.20)	24.32 (3.70)	1.56 (0.27)	Urinary incontinence (72%); decreased sexual desire (44%); decreased sensitivity during intimacy (44%); dyspareunia (24%); hypo/anorgasmia (40%)
G3 (n ¼ 20)	27.20 (2.02)	22.40 (1.27)	1.25 (0.21)	-

BMI ¼ body mass index; PFD ¼ pelvic floor dysfunction.

Quantification of the EMG Signal

The results of sEMG measurements are summarized in Table 2. In general, there are significant differences between the symptomatic groups in comparison with healthy patients. On the other hand, the changes in the measured values after the HIFEM or electrical stimulation were highly statistically significant (P < .001) in comparison with the baseline, showing that stimulation of the PFM modifies the muscle (electrical) activity.

At baseline, measured peak intensity of the MVC signal was significantly higher in healthy patients by approximately 22 mV on average, when compared with that in the G1 or G2 group. At the same time, there was no change between the intervention groups. At the end of study, the G1 group showed significantly higher EMG values than the G2 group (P < .001), reaching an average change of 10.58 mV (57.29%) and 1.44 mV (7.34%), respectively. Although the HIFEM treatment considerably increased the PFM activity, the G1 group still showed lower values than control.

Similar findings were observed in case of average MVC. As expected, the average MVC magnitudes are lower in each group. The more profound increment was also observed in the G1 group (6.65 mV, 58.69%) compared with the modest increase of the G2 group (0.91 mV, 6.81%). There were also significant differences between G1 and G2 groups after treatments (P < .05). Despite the observed improvement, asymptomatic subjects still showed greater EMG values.

Interestingly, the examination of muscle activity at rest revealed divergent tendencies. Initially, only the G1 group showed significantly different (higher) values from control (P < .05) while after the last therapy, the G1 average resting level decreased at the level of G3 (2.08 mV and 1.90 mV, respectively).

Conversely, the average resting level of the G2 group had risen from 2.42 mV to 3.94 mV. In conclusion, the G2 subjects manifested significantly higher EMG values than the control and G1 group at the end of study (P < .001).

In terms of endurance, there were observed significant differences between both the symptomatic groups and either control group at the baseline and after the treatments (see Table 2). The measurement of the G3 group showed that healthy patients were able to hold contraction of the PFM on average for 62.25 s. Furthermore, we observed a significant increase in endurance of PFM contraction by 48.24% in the G1 group because the patients have been able to hold a contraction by 13.44 s longer after their treatments, reaching 41.30 s in total. The G2 group improved by 36.26%, and PFM contraction was prolonged on average by 6.60 s.

Pelvic Floor Impact Questionnairee Short Form 7

Patient's subjective evaluation is summarized in Table 3 and Figure 1. The minimal variation in the baseline score of both symptomatic groups was insignificant. Nonetheless, after the last treatment, there was an observed significant difference in the PFIQ score between the G1 and G2 group (P .01). Although both treatment modalites resulted in highly significant subjective improvement, the patents treated with HIFEM experienced greater outcomes. In additon, 16 patients (35.56%) from the G1 group reached a score of zero after the HIFEM treatments (meaning 100% improvement against the baseline). Contrary to this, only 3 patents (12.00%) from the G2 group, who underwent electrical stmulaton, reported zero score at their last visit.

The shif in PFIQ scores is visualized in Figure 1. As can be seen, the relative frequency of scores was remarkably changed in the G1 group while almost 90% of patents fall into the lowscore categories (0e10 or 10e20) after the treatments. In additon, the scores more than 50 were entrely eliminated from patent's responses. The G2 group showed only minimal changes in distribuon of patent's PFIQ scores, corresponding to a moderate average improvement of 5.15 points (see Table 3).

Discussion

Our examinaton of PFM electrogenesis in patents, who showed signs of PFD, revealed a signifcant reducton of the generated EMG signal in comparison with the asymptomatc patents at baseline (MVC, mean MVC, and endurance). The results of interventon groups G1 and G2 denote that noninvasive PFM strengthening is able to positvely influence the actvity of the PFM. As seen in Table 2, the sEMG measurements obtained afer therapies with the BTL EMSELLA device or electrical stmulaton showed increased values of maximum possible voluntary contracton and endurance. It suggested that at the end of study, patents were capable of stronger and more complex PFM contractons resultng in reducton of PFD symptoms (whether incontnence or sexual based), demonstrated also by signifcant decrease in the PFIQ-7 score.

Tab. 2. Results of the sEMG measurements at the baseline and after the last therapy for both treated groups (G1 and G2) and control subjects (G3) presented as mean followed by 95% confidence interval in brackets

	Peak MVC (mV)		Average MVC (mV)		Resting level (mV)		Endurance (s)	
Group	Baseline	After	Baseline	After	Baseline	After	Baseline	After
G1 (n ¼ 50)	19.49†(2.31)	30.06 †*** (3.75)	11.33† (1.54)	17.99†,* (2.50)	3.83†,* (0.82)	2.08 (0.38)	27.86†,** (4.17)	41.30†,*** (5.21)
G2 (n ¼ 25)	19.56† (2.93)	21.00†(2.82)	13.39† (2.46)	14.30†(2.42)	2.42 (0.45)	3.94†,*** (0.60)	18.20†(2.85)	24.80 †(3.12)
G3 (n ¼ 20)	41.96 (2.51)	-	32.69 (1.88)	-	1 90 (0 63)	-	62.25 (3.68)	-

*EMG ¼ electromyography; MVC ¼ maximal voluntary contraction; sEMG ¼ surface electromyography. Significantly different results (P ≤ .002) against control are depicted by and * denotes significantly higher EMG values for comparison of G1 and G2. *P < .05, **P < .01, ***P < .001.*

In contrast to sEMG measurements, which demonstrated considerable PFM weakening in the G1 and G2 group at baseline, the PFIQ resulted in relatvely low scores in both groups. We atribute this to perhaps a less specifc grading system of the PFIQ, when evaluatng patents who showed a various range of PFD-related symptoms of diferent severity. In future studies, it might be benefcial to focus on the evaluaton of partcular patent's symptoms by using conditon-specifc questons evaluated by a visual analogue scale or 5 to 7-point Likert scale for instance to enhance grading possibilites.

Comparison of the Magnetic and Electrical Stimulation

Signifcantly, greater improvement in EMG values was observed in the G1 group, treated by HIFEM technology. In comparison with electrical stmulaton, the BTL EMSELLA device showed to be substantally more efectve in restoraton of muscle strength as the MVC, mean MVC, and endurance parameters uniformly increased ranging from 48 to 59% afer HIFEM treatments. On contrary, electrical stmulaton induced only mild changes in MVC (7.34%) or mean MVC (6.81%) while reaching mild to moderate improvement (36.26%) of endurance.

The sEMG measurements coincide with the results of the PFIQ. Patent's subjectve evaluaton showed more pronounced improvement in the G1 group (57.16%) than in the G2 group (32.18%), which corresponds to the improvement rate in EMG values. The HIFEM procedure also resulted in substantal reducton of high PFIQ scores afer the last therapy session (see Figure 1).

PFM Electrical Activity and sEMG Measurements

Given the specific patient group and scarce evidence in literature, control group G3 was established to obtain normative EMG values, valid for the studied sample. In general, herein presented results coincide with the previously published findings. It has been documented by numerous authors[13e15,17,18,20] that women who are suffering from PFD show lower MVC and endurance values because of the impairment of the PFM. By the proper stimulation of the PFM, patients are able to produce greater voluntary contractions for longer durations. In addition, the muscle activity at rest is influenced by the PFD as the PFMs are less electrically active. However, the evaluation of the PFM resting level revealed significant differences between both modalities in our study. Although the G1 group after treatments reached similar EMG values as healthy population, patients from group G2 showed altered muscle activation with relatively high electromyogenesis at rest (3.94 mV on average, see Table 2). This indicates that G2 patients cannot properly relax their PFM after treatments because they are not able to isolate and control the appropriate muscle activation patterns, which was then reflected by the lower MVC amplitudes. The correct activation pattern during PFM contraction is associated with increased activation of the PFM and lower transverse abdominal wall with markedly less activation of the upper abdominal and chest wall. The inappropriate activation refers to an increased level of abdominal and chest wall activation while PFM activation decrease,[16] resulting in lessened strength (MVC amplitude) of contraction.

Showing high test-retest reliability,[13,14] the sEMG measurement is a useful tool for detection of PFM activity. For recording of PFM electrical activity, we used an intravaginal electrode with a large surface to obtain EMG signals of sufficient amplitude with high sensitivity.[2,3] Fortunately, the PFM encompasses only a partial amount of subcutaneous tissue which may possibly further attenuate the amplitude of EMG.[35] To prevent any systematic error during measurements, insertion and the position of the measuring electrode was supervised by the skilled physiotherapist. The normalization of data was not considered necessary as we assessed the same muscle group during one measurement session without removal of the active electrode.[3]

The selectivity of measured values was accomplished by the reference electrode, placed on the abdomen. The signal obtained by the abdominal electrode was subtracted from the recording site to eliminate common components, and received EMG values thus represented summation activity of the whole PFM. To achieve an even greater degree of selectivity, the specific design of the vaginal electrode is required. For instance, Voorham-van et al[14] have been able to successfully measure and compare the activity of selected pelvic muscles (pubococcygeus, puborectalis, bulbospongiosus and ischiocavernosus) by using experimental intravaginal probe with a matrix of 24 electrodes.

Study Limitations

Still, a sEMG measurement faces various challenges. The nature of the recorded electrical signal (amplitude, frequency or noise) is influenced by several factors, such as composition of measured muscle along with structure and position, or placement of electrodes.[35] The core and skin temperature[36] or different humidity of measured environments may also influence the signal

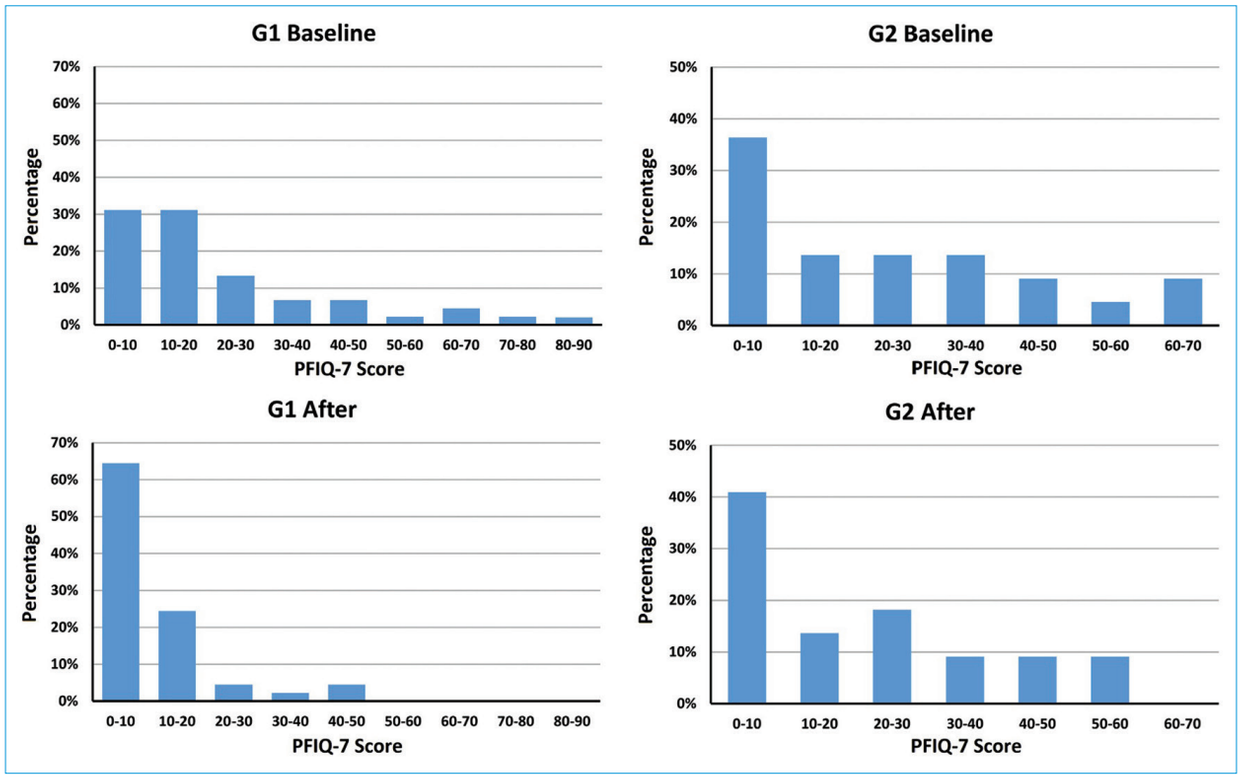

Fig. 1. The comparison of PFIQ-7 scores per group and appointment. The relative frequencies of scores reported by the patients of group 1 (G1) and group 2 (G2) are plotted in the graphs. There is a substantial shift toward the lower PFIQ-7 scores in the G1 group after the treatments.

parameters. Because of the moisture and temperature within the vaginal lumen, it is difficult to ensure identical conditions at each visit during the intravaginal measurements. Especially, the moisture between the electrode and tissue may lead to decreased EMG amplitude. Furthermore, the electrode positioning is crucial for reliability of sEMG measurement. Therefore, the operator must insert the intravaginal probe consistently with respect to the measured muscles as the power of the signal is affected by the electrode orientation.[37] In addition, the intravaginal probes should be designed in such a way to minimize any impact on the PFM by its insertion to avoid cross talk and motion artifacts.[14]

Indisputably, the appropriate planning of treatments is essential to achieve desired results. Unlike the electrical stimulation, HIFEM is relatively new technology which is still being investigated to some extent. In our study, the HIFEM treatments were administered at least 48 hours apart (2e3 per week) to maximize treatment outcomes but also to avoid muscle fatigue, caused by overtreatment of the PFM, as the therapy with maximum settings produces intense muscle contractions. Presumably, the results would differ because of changes of the treatment frequency; however, this should be verified by future studies.

Conclusion

Electromyographic measurement of PFM activity proved to be a valid method for examination of patients with PFD (suffering from urinary incontinence and/or accompanied with sexual dysfunction) treated with HIFEM and electrical stimulation. Surface EMG of the PFMs showed

more profound muscle activation after HIFEM treatments along with improved relaxation and enhanced endurance. As well, the PFIQ indicates greater effect of HIFEM procedure based on the significant change of score reported by patients. Documented outcomes imply that the HIFEM procedure is substantially more effective in restoration of PFM strength and treatment of PFD when compared with the electrical stimulation, applied correspondingly in postpartum women.

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Dr. RAOUL ORVIETO
The Tarnesby-Tarnowski Chair for Family Planning and Fertility Regulaton,
Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

DURING THE CORONAVIRUS DISEASE 19 (COVID-19) PANDEMIC, WE ENCOUNTERED SEVERAL CLINICAL DILEMMAS THAT NEEDED TO SOLVED

1. Whether COVID-19 infecton afects the subsequent in vitro fertlizaton (IVF) cycle outcome.
2. Whether mRNA SARS-CoV-2 vaccine afects the subsequent IVF cycle outcome.
3. Whether mRNA SARS-CoV-2 vaccine afects semen analysis parameters in fertle males.
4. Whether mRNA SARS-CoV-2 vaccine afects AMH level.
5. Whether patents' immunizaton following COVID-19 infecton or mRNA SARS-CoV-2 vaccine afects endometrial recepvity, as assessed by their performance in frozen-thawed embryo transfer (FET).

To challenge these dilemmas, we conducted a series of studies testng the impact of COVID-19 infecton and the mRNA vaccines on fertlity in both women and men. While COVID-19 vaccinaton had no efects on IVF treatment/ovarian reserve, gametes/embryos quality, nor endometrial recepvity, COVID-19 infecton was shown to detrimentally afect gametes/ embryos quality, especially if treatment was commenced within 3-6 months following recovery, with no efects on IVF treatment/ ovarian reserve.

Dr. REVAZ BOCHORISHVILI
Ph.D., MD Professor, Obstetrician-Gynecologist, Laparoscopic Surgeon

ENDOMETRIOSIS AND INFERTILITY

Nowadays there is a huge question about surgical treatment of endometriosis, but the main thing is, that the ovaries have to stay functionally active. There are a lot of pro and contra arguments.

The favors of surgery are: reducing pain, removing the risk of ovarian cancer, removing the risk of infection during IVF and treating infertility. But the arguments that speak against surgical treatment of endometriosis, the first comes infertility itself.

During cystectomy, rate of removal of normal ovarian cortex is between 6-50% (Muzii et al.2002; Hachisuga et al 2005), in France – >90% (Roman et al. 2010; Dogan et al 2011). Also some people have doubts about the benefits and needs of the surgery. Also there's a poor outcome of IVF. It works harmful on ovarian reserve markers, especially on Ant-Mullerian Hormone (AMH). There's an evidence deriving from evaluation of serum AMH level modifications after surgical excision of endometriomas supports a surgery-related damage to ovarian reserve. Especially, when the AMH level in serum was low before the surgery.

Some studies say, that laparascopic aspiration or cystectomy of endometriomas prior to ART did not show evidence of benefit over expectant management with regarding to the clinical pregnancy rate.

The risk factors of the surgery but most dangerous are age >38, low AMH/AFC and multiple and bilateral endometriomas. Also second surgery for recurrent endometriomas are the most harmful.

ESHRE guidelines inform, that in fertile women with ovarian endometrioma >3cm surgeons should perform excision of endometrioma capsule instead of ablative surgery that is drainage and electrocoagulaton of the endometrioma wall since it increases the spontaneous postoperative pregnancy rate. Also it is really important, that patents have to be informed about the risks of procedure, for example reducing of ovarian reserve and losing the ovary/ovaries.

Italian physicians have investgated the insert of endometrioma and its toxic efects, which includes oxidative stress, fbrosis of the ovaries, decreasing maturaton of follicles and ect.

That's why the surgical treatment of endometriosis is still golden standard.

Some studies show, that in patents with endometrioma AMH level is already low and afer surgery, ovaries recovered and the AMH serum level was higher, than before procedure. But, unfortunately it happens very rarely. It really depends on the quality of the surgery. The level of expertse in Endometrial Surgery is inversely correlated with amount of ovarian tssue inadvertently removed with the endometrioma wall. In experienced hands, laparascopic stripping of endometriomas appears to be a technique that does not signifcantly damage the ovarian tssue.

Recurrent endometriomas does not mean, that the surgery was done in "wrong hands" – quiet opposite: it means, that during procedure the ovarian cortex was minimally removed.

He also mentoned, that it is really important to reduce using electrocoagulaton during the procedure.

But stll, the main topic for the surgeon is – endometrioma must be operated only once.

International Conference "Infertility 35+ "

1 February, 2020

9:00 - 10:00 | Registration

I SECTION

Chairman: **ARCHIL KHOMASURIZE**
Moderator: **NINO MUSERIDZE**

10:00 - 10:15 | Opening ceremony. Welcome addresses

ARCHIL KHOMASURIDZE (GEORGIA)
MD, Ph.D., Professor, President of Georgian Reproductive Association.

10:15 - 11:15 | Poor Responders

DOV FELDBERG (ISRAEL)
MD, Ph.D., Gynecologist, Reproductologist, Co-Chairman Reproductive Endocrinology & Infertility (REI), Committee of International Federation of Gynecology and Obstetrics (FIGO).

11:15 - 11:45 | ART 35+

VLADISLAV KORSAK (RUSSIA)
MD, Ph.D., Professor
General Director of ICRM (International Center of Reproductive Medicine.
President of Russian Association of Human Reproduction (RAHR),
ESHREEIM Community Council member.

11:45 - 12:30 | *Coffee break*

II SECTION

Chairman: **ARCHIL KHOMASURIDZE**
Moderator: **NINO MUSERIDZE**

12:30 - 13:00 | Endometrium and ART Outcomes

VLADISLAV KORSAK (RUSSIA)
MD, Ph.D., Professor

13:00 - 13:30 | Micro TESE

IVAN HOFFMANN (GERMANY)
MD, Ph.D, Urologist, Secretary of the German Society of Andrology (DGA),
Berlin Andrology Center

13:00 - 13:45 | Sperm DNA fragmentation: where and how it occurs?

ALEKSANDER KHELAIA (GEORGIA)
Md, Ph.D., Urologist, National Center of Urology,Tbilisi, Georgia.
Associated Professor of European University.
Co-chair of Androlgy section of Georgian Urological Association,
EAU Section of Andrological Urology member (ESAU)

13:45 - 14:00 | Study cases in IVF

TAMAR MAGULARIA (GEORGIA)
MD, Ph.D., Reproductologist, Georgian-German Reproductive Center.

NINO MUSERIDZE (GEORGIA)
MD, Ph.D., Embryologist,
Clinical Director of Georgian-German Reproductive Center.

14:00 - 14:30 | Infertility and Thrombophilia

DOV FELDBERG (ISRAEL)
MD, Ph.D.

14:30 - 16:30 | *Lunch*

DOV FELDBERG (ISRAEL)
MD, Ph.D.

III SECTION

Chairman: **TENGIZ ASATIANI**
MD, Ph.D., Professor,
Chairman of Georgian Obstetrician's and Gynecologists Association.
Moderator: **NINO MUSERIDZE**

16:30 - 17:00 | Genetic Test in Reproductology

GÜLAY ÖZGÖN (TURKEY)
MD, Ph.D., Genetcist, Nesiller Genetk Tanı Merkezi.

17:00 - 17:30 | Discuss the book

Authors: **VLADISLAV KORSAK, NINO MUSERIDZE**

17:30 - 18:45 | Workshop - „Embryotransfer"

SEMRA SERTYEL (TURKEY)
MD, Embryologist, Head of IVF Department of Medical Park.

YASHAR TAYFUN ALPER (TURKEY)
MD Ph.D., Reproductologist, IVF Department of Medical Park.













ERENCE AND WORKSHOP
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1 FEBRUARY, 2020
TBILISI, GEORGIA







2nd International Conference "Infertility 35+"

12-13 June, 2021, Tbilisi, Georgia

12/06/2021 Day 1

8:30 - 9:00 | Registration

I SECTION
9:00 - 12:00

Chairman: **ARCHIL KHOMASURIDZE**
Moderator: **NINO MUSERIDZE**

9:00 - 9:20 | Opening ceremony. Welcome addresses

ARCHIL KHOMASURIDZE (GEORGIA)
MD, Ph.D. Professor, President of Georgian Reproductive Association

9:20 - 9:40 | Micro TESE State of the Art

IVAN HOFFMANN (GERMANY)
MD, Urologist, Andrologist, Europian Academy of Andrology EAA,
Secretary of the German Society of Andrology (DGA),
Berlin Andrology Center

09:40 - 10:00 | The Role of LH for Ovarian Stimulation 35+

ROBERT FISCHER (GERMANY)
MD, MVZ Fertility Center Hamburg GmbH,
Medical Director, Reproductive Endocrinologist

10:00 - 10:20 | Overcoming Infertility of Women in Older of Reproductive Age. Is the Result of ART Predictable?

VYACHESLAV LOKSHIN (KAZAKHSTAN)
Professor, Academician of the National Academy of Sciences of the RK,
President of the Kazakhstan Association of Reproductive Medicine (KARM), CEO of the ICCR "PERSONA"

10:20 - 10:40 | Is There a Place for Gestagens in the Stimulation of Superovulation in IVF Programs

SHOLPAN KARIBAYEVA (KAZAKHSTAN)
Candidate of Medical Sciences, Reproductologis,
Director for Strategic Development of the ICCR "PERSONA"

10:40 - 11:00 | Covid 19 and ART

VLADISLAV KORSAK (RUSSIA)
MD, Ph.D., Professor, General Director of ICRM.
President of Russian Association of Human Reproducton (RAHR),
ESHREEIM Community Council member

11:00 - 11:20 | "Pure" IVM has Opened the Way to a "Peaceful" Consensus in the Collaboration of an Oncologist and a Reproductologist! Experience of St. Petersburg

MAKA OSEPAISHVILI (RUSSIA)
MD, Ph.D., Obstetrician-Gynecologist, Reproductologist, NGC St. Petersburg

11:20 - 11:40 | ART in Women of Late Reproductive Age

NATO SHAMUGIA (RUSSIA)
MD, Ph.D., Associate Professor of the Department of Obstetrics and Gynecology, RMANPO, Medical Director of the GMS IVF Clinic, obstetrician-gynecologist, reproductologist, Member of the Education Committee of the Russian Association of Human Reproduction (RAHR)

11:40 - 12:00 | IVF. How Not to Turn Your Last Hope into a Missed Opportunity

TAMARA NADIRASHVILI (GEORGIA)
MD, Ph.D., Obstetrician-Gynecologist, Reproductologist, Georgian-German Reproductive Centre (GGRC)

12:00 - 12:20 | *Coffee break*

II SECTION
12:00 - 14:00

12:20 - 12:40 | How is IVF Done at GGRC Clinic

VENIAMIN KAZARINOV (RUSSIA)
Embryologist, Head of Embryo Laboratory, Georgian-German Reproductive Centre (GGRC)

12:40 - 13:00 | PGT in Clinical Practice

EKATERINA POMERANTSEVA (RUSSIA)
MD, Ph.D., Genetic Laboratory, GMS Clinic

13:00 - 13:20 | Long-Dreamt Pregnancy and Then...

MAKA GEGECHKORI (GEORGIA)
MD, Ph.D., TSMU Professor, Zurab Sabakhtarashvili Reproductive center Head of Medical science department, Head of Association Georgian Gynecology and Endocrinology

13:20 - 13:40 | Fertility Preservation In Cancer Patients

FOAD AZEM (ISRAEL)
MD, Director - IVF Unit, Lis Maternity Hospital

13:40 - 14:00 | Advanced Maternal Age (up to 35) Require Advance Lab Technologies

BIROL AYDIN (TURKEY)
Head of Embryology laboratory, Leading clinic embryologist and management consultant

14:00 -15:00 | *Lunch*

III SECTION
15:00 - 16:30

15:00 - 15:20 | Estrogen Deficiency and Modern Principles of management

JENARO KRISTESASHVILI (GEORGIA)
MD, Ph.D., Vice president of Georgian Association of Reproductive Health, Professor of TSU Medicine School, Deputy chief of

Reproductive Medicine Center Universe, Associated member of Human reproduction International Academy

15:20 - 15:40 | Expert Approach for Oocyte Donation

ULIANA DOROFEYEVA (UKRAINE)
MD, MRCOG, Medical Director OVOGENE Egg Bank,
Founder of Ukrainian Association of Medical Transportation "Biotransfer",
Expert Advisor of IVF Media

15:40 - 16:00 | Sperm Aneuploidy and Infertility

ALEKSANDRE KHELAIA (GEORGIA)
MD, PhD Urologist, National Center of Urology.
Professor of European University, Co-chair andrology section of
Georgian Urological Association

16:00 - 16:20 | Ovarian Stimulation in PCO Patents in ART

BOTROS RIZK (USA)
MD, MA, FACOG, FACS, HCLD, FRCOG, FRCS, Professor of Obstetrics
and Gynecology and the head of Reproductive Endocrinology
and Infertility and Medical and Scientific Director of In Vitro Fertilization
and Assisted Reproduction at the University of South Alabama,
Lab Director to Odessa fertility lab at Odessa Regional Medical center.
Faculty member at Texas Tech University in Odessa, TX

16:20 - 16:40 | ERPeak and Personalized Embryo Transfer

TAMAR BADRIDZE (USA)
MD, NYC IVF, New York, USA

16:40 - 17:00 | *Coffee break*

IV SECTION
17:00 - 18:30

17:00 - 17:20 | Corona Pandemic will End But Old, Familiar Viruses will Remain

MADONA JUGELI (GEORGIA)
MD, Ph.D., Gynecologist-reproductologist, President of
the Federation of Colposcopy of Georgia

17:20 - 17:40 | Ovarian Endometriosis and Reproduction: Is Surgery Necessary?

REVAZ BOCHORISHVILI (FRANCE)
Ph.D., Professor, MD, Obstetrician-Gynecologist, laparoscopic Surgeon.
Director of the International Centre of Endoscopic Surgery (CICE)
and Head of the Diagnostic and Treatment Centre of Endoscopic Surgery
of Policlinique de Hotel-Dieu (France), Head of gynecological department
of the Centre Hospitaller Universitaire Clermont-Ferrad

17:40 - 18:40 | *Discussion*

18:40 - 19:00 | Presentation of the new Magazine of GGRC

NINO MUSERIDZE (GEORGIA)
MD, Ph.D., Clinical Director of Georgian-German Reproductive Centre (GGRC)

13/06/2021 **Day 2**

9:30 - 10:00 | Registration

Workshop - Preliminary Registered Participants only

10:00 - 10:15 | Conference Conclusion

ARCHIL KHOMASURIDZE (GEORGIA)
MD, Ph.D. Professor, President, Georgian Association of Reproductive Health

10:15 - 10:30 | Legal Aspects of surrogacy and donation

GIORGI ARCHVADZE (GEORGIA)
General Director of Georgian-German Reproductive Centre

10:30 - 12:00 | Round Table - Actual Topics in the Reproductive medicine, Regional experiences

VALERIA AGLONIETE (LATVIA)
Gynecologist, Medical Director of "Your doctors" privet clinic,
Head of Latvian Human Reproduction Society,
Chairman of the board of Baltic society of reproductologists

VIYACHESLAV LOKSHIN (KAZAKHSTAN)
Professor, Academician of the National Academy of Sciences of the RK,
President of the Kazakhstan Association of Reproductive Medicine
(KARM), CEO of the ICCR "PERSONA"

12:00 - 12:15 | *Coffee break*

12:15 - 12:40 | Round Table - Actual Topics in the Reproductive medicine

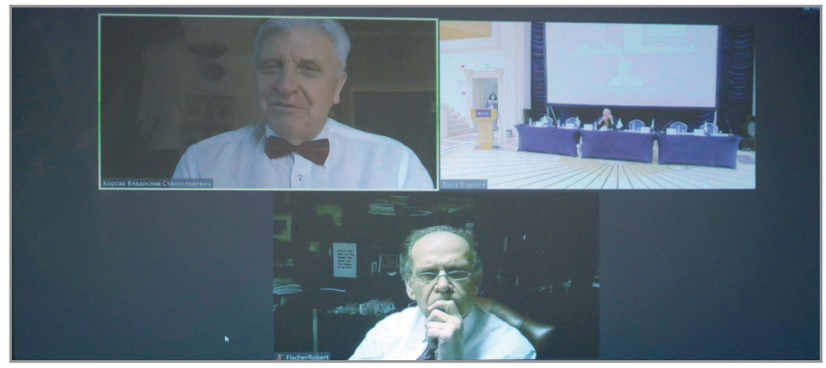
NATO SHAMUGIA (RUSSIA)
Member of the Education Committee of the Russian Association of
Human Reproduction (RAHR), member of the Scientific Committee of
the Association of Gynecologists, Endocrinologists and Therapists

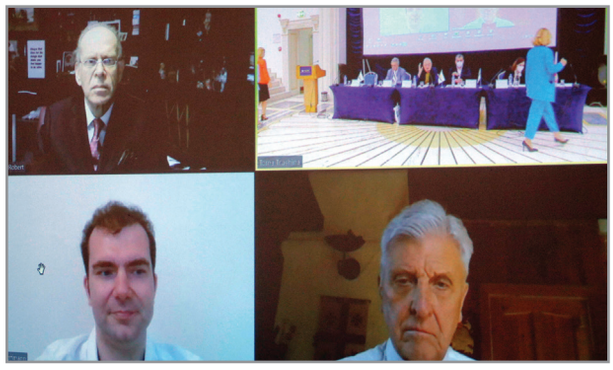
12:40 - 14:00 | *Discussion*

14:00 - 15:00 | *Lunch*

15:30 - 18:30 | *Tbilisi Sightseeing Tour*

19:00 - 20:45 | *Dinner in the Hotel*



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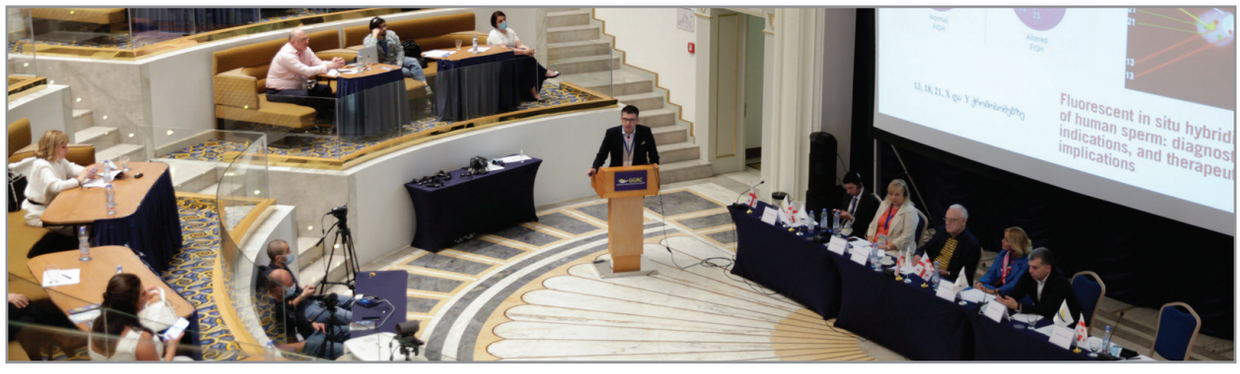
Fluorescent in situ hybrid
of human sperm: diagnost
indications, and therapeu
implications

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