Reproductive disorders in men are the cause of infertility of 30–40 % of infertile couples. The genetic factors play a great role in male infertility as they are detected in 15–30 % of men. The distributions of polymorphic variants of candidate genes relevant to male fertility in different populations are of great interest to explain the male idiopathic infertility. The aim of this study was to explore the association of the SEPS1 gene polymorphism G-105A (rs28665122) with pathospermia in infertile men in Moscow region. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to detect SEPS1 G-105A polymorphism in 26 cases and 24 controls. The results showed that the frequency of the minor allele A of gene SEPS1 is higher in men with pathospermia than in the control group of fertile men. Conclusion: The SEPS1 gene polymorphism G-105A is associated with idiopathic infertility in men with pathospermia and can be used to screen idiopathic infertility in men.

Keywords: idiopathic male infertility, genetic factor, gene SEPS1, G-105A polymorphism
Reproductive disorders in men are the cause of infertility of 30–40% of infertile couples [1, 2, 4]. Spermatogenesis is a complex biological process that depends on the precisely controlled cascade of activation and deactivation of certain genes [3]. The process of spermatozoa maturation from precursor cells (spermatogenesis) is the result of the expression of these genes. In humans, more than 2000 genes are involved in this process [7, 10]. Therefore, genetic infertility is detected in 15–30% of men [2, 5, 6]. The most studied genetic factors for male infertility are alterations in the chromosomes level (chromosome aberrations), at the level of gene or a group of genes (mutations), at the level of total DNA (chromatin dispersion and DNA fragmentation) [3, 9]. Due to genetic disorders, there may be different forms of infertility in terms of their etiology and severity: from minor spermatogenesis disorders to total gonadal dysfunction [9]. That is why the study of genetic factors associated with an increased risk of male infertility requires the knowledge of the population-specific characteristics of the frequency of distribution of genotypes and alleles of candidate genes. To study the association of G-105A (rs28665122) polymorphism of SEPS1 gene with the development of pathospermia in men with infertility in the Moscow region.

Material and Methods. The study involved 26 patients (the first group) with different forms of pathospermia (idiopathic form) and 24 fertile men (the second group) with one or more children. The mean age of the patients was 30±2 years, the mean age of fertile men was 29±4 years. The study group included patients whose wife’s reproductive viability was confirmed clinically.

Genomic DNA for genetic analysis was isolated from peripheral blood leukocytes using «DNA-express-blood» kits produced by LLC Synthol. All DNA samples were tested for the presence of G-105A (rs28665122) polymorphism of SEPS1 gene using polymerase chain reaction (PCR) and subsequent analysis of restriction fragment length polymorphism (RFLP). For the PCR analysis, a «Tercik» (by DNA technologies) thermo cycler was used to identify the site containing the G-105A polymorphism of the SEPS1 gene. The following primers were used in the study [4]: 5'-TCCTTGCTCATGTTCCAAT-3'; 5'-GCCGACAGACTCTCTTT-3'. PCR was carried out in 25 μl of a reaction mixture containing 20 ng of DNA, 0.2 μl of each primer. Homozygotes GG correspond to 370 bp DNA fragment, AA homozygotes – 233 and 137 bp fragments. Heterozygotes AG contain all three fragments. Heterozygotes AG contain all three fragments.

Statistical analysis was carried out using MS Excel (Microsoft, USA) spreadsheet tables and the STATISTICA 6.0 (Statsoft, USA). The differences were considered significant when p<0.05.

Results and Discussion. All patients of the first group suffered from severe infertility and participated once with negative result in the ART program (assisted reproductive technologies). The patients had different forms of pathospermia confirmed by spermogram analysis. Of these, asthenozoospermia was founded in 12 (46.1%) patients (motility of A+B spermatozoa types was 11.5±9.7%), 9 (34.6%) men had teratozoospermia (pathological forms of spermatozoa 85±14.3%), in 5 (19.3%) – azoospermia were founded. The results of the clinical examination (biochemical blood test with hormonal profile, prostate secretion analysis, urethral smear, karyotyping, scrotal ultrasound, etc.) did not reveal any detectable abnormalities. Thus, we recorded idiopathic male infertility in the patients of the first group.

A comparison of the results of genetic testing of the patients and fertile men to detect the distribution of SEPS1 gene polymorphism is presented in Figure.

![Fig. Frequency of the distribution of G-105A polymorphism of SEPS1 gene in patients with infertility and fertile men in the Moscow region](image)

Studies of the distribution of SEPS1 gene polymorphism showed that among patients with pathospermia, allele A carriers were revealed almost twice as often (p<0.05) as in the control group of fertile men (65.4% and 35.5%, respectively). The frequency of the minor allele A was significantly higher (p<0.05) in patients with infertility than in the group of fertile men (36.5% and 18.7%, respectively).

The results obtained in our studies are consistent with the data received by other authors who studied the relationship of this polymorphism with the risk of the development of a number of diseases [7, 8].

The human genome contains 25 genes encoding the synthesis of selenocysteine-containing proteins – selenoproteins. These proteins are involved in numerous intracellular processes, including regulation of reductive-oxidative cell homeostasis. Selenoprotein S belongs to the group of membrane proteins that control the stress response to activation of the inflammatory cascade in the endoplasmic reticulum and protects the functional integrity of the endoplasmic reticulum from the destructive effects of oxidative stress [5, 9]. In a number of the other papers, the correlation of G-105A (rs28665122) polymorphism of selenoprotein S SEPS1 gene with increased expression of cytokines and the development of pathological conditions inflammatory in nature associated with the risk of premature birth in women [9] and the risk of the development of cancer and autoimmune diseases in some Asian and European populations [7, 8].

Since the studies of G-105A (rs28665122) polymorphism of the SEPS1 gene in the Russian Federation have not been performed earlier, it seems to be essential to study the association of this polymorphism with the development of pathospermia among men in the Moscow region (Figure).

Conclusions. G-105A polymorphism of SEPS1 gene was revealed twice as often in patients with infertility compared to fertile men. A small patients sample does not allow us to provide a reasonable estimate of the results obtained, further investigations are there necessary to do the conclusion. However, if the correlation of G-105A polymorphism of SEPS1 gene...
with the risk of the development of pathospermia will be established, this polymorphism can be considered as a new genetic factor of the prognosis for men with infertility (reproductive disorders). The obtained results indicate the effectiveness of study the G-105A polymorphism of SEPS1 gene for the development of idopathic infertility in men, for regarding reproductive potential for the patient and the selection of appropriate management.

Disclosures:
The authors declare no conflict of interest.

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STUDY OF PAIN IN NEWBORNS

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ISCHESEĐOVANIE BOLI U NOVOROЖДЕННЫХ

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Evaluating the pain response in children is difficult. Nevertheless, the search for methods with which to assess pain objectively in newborns with surgical pathology of the digestive tract remains urgent. Therefore, we conducted a study of the serum concentrations of pain markers (substance P and neurokinin A) in infants to determine the relation of each of these