

UDK 618.177-089.888.11(571.56)

**Effectiveness of superovulation induction in indigenous  
and non-native women with tubal-peritoneal infertility,  
living in the Far North**

**Semenova A.A., Bustritskaia T.S.**

**Summary:** There are submitted the results of superovulation stimulation in 30 native women of the North (the main group) and in 27 non-native women (the comparison group) with tubal-peritoneal infertility. In the main group the ovarian response to gonadotropin stimulation is diminished, the number of preovular follicles and oocytes are less than in the comparison group, the embryos development in vitro is slowed and the pregnancy rate in the program of In Vitro Fertilization (IVF) is almost 3 times lower. The use of superovulation stimulation protocols with GnRH-A in the main group increases the effectiveness of IVF by a factor of three.

**Key words:** infertility, ovulation stimulation, effectiveness of In Vitro Fertilization.

In the structure of infertility the tubal-peritoneal factor makes up 40-72% [4]. One of the main methods of treatment of tubal-peritoneal infertility is IVF [2]. Nowadays, indications for IVF, including infertility, not treatable by therapy, and higher efficiency of IVF as compared with other methods are determined. It should be noted, that the problem of increasing the effectiveness of IVF is still topical and requires more thorough studies [6]. Standard protocols of ovarian stimulation in IVF programs are well-developed, but the specialists' attention focuses on the possibilities of optimizing them according to the individual peculiarities of each concrete patient.

**The purpose of the study** was to explore the possibility of increasing the effectiveness of IVF programs in native women of Yakutia, living in conditions of the Far North.

**Materials and methods**

The study involved 57 women with tubal-peritoneal infertility who had indications for IVF. The main group consisted of 30 native women of the North and the comparison group - 27 non-indigineous women. Exclusion criteria were contraindications for superovulation induction and surgical interventions on the ovaries. Depending on the used schemes to stimulate ovulation

the following subgroups were identified: Subgroup 1 – of 15 women from the main group, whose ovulation was stimulated according to the scheme with the use of drugs, consisting of Gonadotropin Releasing Hormone-Agonist and Human Menopausal / Recombinant Gonadotropin (GnRH-A + HMG/rFSH) – Long protocol; Subgroup 2 – of 15 women from the main group whose ovulation was stimulated according to the scheme with the use of drugs of Human Menopausal/ Recombinant Gonadotropin and Gonadotropin-Releasing Hormone-Antagonists (GnRH-ant + HMG/rFSH) – Short protocol.

The following methods of investigation were used: clinical, hormonal and ultrasound. To determine the ovarian reserve on days 2-3 of menstrual cycle we studied the content of gonadotropins (LH, FSH) and total amount of Testosterone (Total Testosterone) in the blood serum using the test systems "Hema-medina" (Moscow). Ovarian volume and number of antral follicles were determined with the help of the ultrasonic apparatus "Acuson Aspen", using the sensor C9 - 5 MHz for transvaginal study in the two-dimensional gray scale scanning mode.

Stimulation of ovulation in IVF program and embryo transfer (ET) were conducted in 57 women. Dynamic hormonal and ultrasound screening, transvaginal puncture, in vitro fertilization and embryos transfer were performed by standard techniques. The duration of ovulation stimulation and doses of used preparations in the protocols of the examined groups were not significantly different.

The results of the study were processed by a standard software package "Statistica" for Windows 6.0 (Statsoft Inc., USA). To compare the data and evaluate the significance of the results' differences we used t – criterion of Student. Changes were considered statistically evident at the significance level of  $p < 0,05$ .

### **Results of the study**

The average age of women from the observed groups was  $33,4 \pm 4,2$  and  $32,9 \pm 4,4$  years old ( $p > 0,05$ ) respectively. The duration of infertility rated, on the average, from 2 to 14 years: in the main group -  $7,79 \pm 3,6$  years, in the comparison group -  $7,73 \pm 3,06$  ( $p > 0,05$ ). In 60% of women from the main group and in 59,2% patients of the comparison group the infertility was primary. The etiological factor in all cases was tubal-peritoneal.

When analysing the reproductive function it was revealed, that ectopic pregnancy ( $p < 0,05$ ) and its surgical treatment (tubectomy) was 3 times more often in women of the main group (33,3%) than in the comparison one. Chronic salpingo-oophoritis was marked in past history of all women in both groups.

Chronic endometritis was diagnosed in 33,3% of women of the main group and in 13,8% ( $p<0,05$ ) of patients from the comparison group. The frequency of cervical diseases in the form of erosion, cervical dysplasia and chronic cervicitis was higher in the main group. Endometriosis, leiomyoma and polycystic ovary syndrome were more common in women from the comparison group.

The content of FSH, LH in the blood serum of women from the tested groups had no statistically significant differences. In the group of native women the amount of total Testosterone ( $1,3 \pm 0,8$  nmol/L) was lower as compared with the group of non-indigenous patients ( $2,8 \pm 1,0$ ;  $p<0,01$ ), but for all women it was within the age rate.

In women from the main group the number of antral follicles in the right ovary was  $5,4 \pm 2,3$  and in the left ovary –  $4,9 \pm 2,6$ , while in women from the comparison group ( $p<0,05$ ) their number amounted to  $6,7 \pm 2,7$  and  $6,3 \pm 2,6$  respectively. In women of the comparison group the volume of the right ovary was  $8,39 \pm 3,21$  cm<sup>3</sup>, of the left one-  $7,41 \pm 2,42$  cm<sup>3</sup>, that is larger than ovarian volume measured in the main group ( $p<0,05$ ).

When analyzing the processes of follicle-, oocyte - and early embryogenesis (Table) it was found out, that the average number of growing ( $8,1 \pm 5,7$ ;  $p<0,05$ ) and dominant follicles ( $6,7 \pm 5,1$ ;  $p<0,05$ ) was larger in the comparison group. The number of fertilized oocytes did not differ significantly in both groups and amounted to  $3,7 \pm 3,1$  in the main group and  $4,5 \pm 4,2$  in the comparison group ( $p>0,05$ ). The quality of oocytes had an effect on the number of embryos obtained, that was  $1,2 \pm 0,9$  in the main group and  $2,1 \pm 0,9$  ( $p<0,05$ ) in the comparison one. The intensity of cleavage was assessed by the number of blastomeres of embryos on the day of embryo transfer. The analysis of the number of good quality embryos (of 8 blastomeres and blastocysts on the day of transfer) showed that their number was 2 times more ( $1,4 \pm 0,6$ ) among non-native women than in indigenous women ( $0,6 \pm 0,7$ ;  $p<0,05$ ). The number of transferred embryos was on the average  $1,2 \pm 0,8$  and  $1,5 \pm 0,7$  ( $p>0,05$ ) in the groups respectively. Embryos transfer was performed on the third and fifth days of cultivation. On day 5 embryos transfer was conducted in 34% of women from the main group, but only 39% of embryos in their developmental stage corresponded to the day of transfer. In the comparison group 42% of embryos transfer was made, but 64% of embryos were at the stage corresponding to the day of transfer. On the day of embryos transfer the endometrial thickness had no differences in both groups.

In the main group, pregnancy was achieved in 13.3% of cases and in the comparison group – in 37% ( $p<0,05$ ).

Duration of superovulation induction in women with Long protocol was  $10.4\pm 2,9$  days, that was 1,7 days longer than the one in the subgroup with Short protocol ( $p<0,05$ ).

The average number of growing follicles was larger ( $6.23\pm 3.05$ ) in the subgroup using the scheme of stimulation GnRH-a + rFSH/hMG, than using the scheme rFSH/hMG + GnRH-ant ( $4.35\pm 1.93$ ,  $p<0,05$ ). The number of fertilized oocytes was also larger in Subgroup 1 ( $5.62\pm 4.23$ ), than in Subgroup 2 ( $3.06\pm 1.85$ ,  $p<0,05$ ). However, it had no effect on the quality of the fertilized oocytes, as the number of good quality embryos in the examined groups had no statistically significant differences. The average number of the transferred embryos did not differ in the both groups as well and amounted to  $1,5\pm 0,9$  and  $1,2\pm 0,7$  accordingly.

In the main group the pregnancy rate was 10.0% with the use of long scheme of stimulation of ovulation, 3,3% - with the short scheme and in the comparison group - 22,2% and 14,8% respectively. Among non-native women pregnancy was achieved in all age groups, among indigenous women – at early reproductive age group. In the main group pregnancy with twins occurred in one case and ended with operative delivery in time. In the comparison group two cases of twins, resulted in immediate operative delivery, were registered. Tubal pregnancy occurred in one woman in Subgroup 1.

## Discussion

In our study, all women had had inflammatory diseases of the genitals. Purulent process of the uterus, fallopian tubes and ovaries leads to marked functional and morphological disturbances, damage of the receptor system and tissues of these organs. The time for implementation of reproductive plans shortens as a result of early depletion of ovarian function [1].

The possibility of increasing the effectiveness of assisted reproductive technologies is widely discussed in literature [author]. However, reliable criteria, due to which one can predict the possibility of obtaining high-quality oocytes, have not been found yet. We were confronted with a task to study the possibility of increasing the effectiveness of IVF programs in women living in the Far North. Investigation of the parameters of ovarian reserve allowed us to highlight

the most significant ones: volume of ovaries and the number of antral follicles in each of them. The basal FSH level in our study turned out to be statistically insignificant.

The total amount of Testosterone in all women complied with relevant standards. In the group of non-native women the total amount of Testosterone was higher than the one in the group of native women ( $p < 0,05$ ). Recently, there have been data that the poor response is associated not only with the diminution of follicular reserve, but also with the weakening androgen-secreting ovarian function [8]. According to this concept, androgen deficiency inhibits the adequate development of follicles, that creates conditions for poor response by using inducers of ovulation [aut.].

The comparative analysis of follicle-, oocytes- and early embryogenesis revealed that the number of growing and dominant follicles was larger in the group of non-native women. The number of antral follicles being less than 7, indicates poor response to stimulation [3]

We found out the differences in the number of embryos of good quality - non-indigenous women had them in greater numbers than native women. In the induction of superovulation in IVF program achieving pregnancy is the end result.

In the group of indigenous women of the North the pregnancy rate was almost 3 times lower than in the group of non-native patients. The possibilities of increasing the effectiveness of infertility treatment by modifying the schemas of stimulation and, in particular, by the way of using GnRH-ant in Short protocol, are discussed in literature[7]. The analysis of protocols of superovulation stimulation revealed that the duration of stimulation turned out to be not long in the subgroups where GnRH-antagonist was used, that was in line with the other studies [5]. The average number of growing follicles and fertilized oocytes were larger with the use of Long protocol. In the subgroup of women, using the protocol with GnRH-a, pregnancy rate was higher by 3 times.

Comparing the results of treatment of 57 women, we have found that the effectiveness of treatment with IVF is determined primarily by the state of ovarian reserve, which has a negative effect on reproductive function.

## Conclusions

1. Indicators of ovarian reserve (ovarian volume and the number of antral follicles in each of them) are important in the reproductive potential of women and allow to predict the possibility of pregnancy during conducting IVF.

2. In native women of the North the ovarian response to gonadotropin stimulation is poor, the number of preovular follicles and oocytes are less than in non-indigenous women, the development of embryos in vitro is slow and the pregnancy rate in IVF programs is almost 3 times lower than the one in non-native women.

3. The use of protocols of superovulation stimulation with GnRH-a in native women of the North increases the efficiency of IVF by 3 times as compared with protocols using GnGR-ant.

Table

**Sonographic parameters of superovulation stimulation  
in IVF program**

Parameters	Main group (n=30)	Subgroup 1		Comparison group (n=27)
		(n = 15)	2-я (n = 15)	
The number of growing follicles	5,1±2,6*	6,2±3,0**	4,3±1,9	8,1±5,7
The number of dominant follicles	4,5±2,5*	5,3±3,2**	3,9±1,5	6,8±5,2
The number of fertilized oocytes	3,7±3,1	4,6±4,2	3,1±1,8	4,6±4,3
The number of embryos	1,3±0,9*	1,1±0,7	1,4±1,1	2,1±0,9
The number of “good” embryos	0,6±0,7*	0,4±0,7	0,7±0,7	1,4±0,7
The number of transferred embryos	1,2±0,8	1,2±0,9	1,2±0,7	1,5±0,7

\* -  $p < 0,05$  statistical significance of differences between the main group and the comparison group;

\* \* -  $p < 0,05$  - statistical significance of differences between the 1-st and 2-nd subgroups.

## References

1. Buyanova S.N. Reproductive prognosis in patients with purulent inflammatory diseases of the pelvic organs: problems and solutions / S.N Buyanova, N. A. Shchukina, A.V. Gorshilin // Russian Journal of obstetrician - gynecologist. - 2009. - № 2. - S. 67.
2. Korsak V.S. The study of the endometrium in women with tubal-peritoneal infertility at the stage of preparation for IVF / V.S. Korsak, O.V Zabelkina, E. V. Isakova, A.A. Kirsanov // Problems of reproduction. - 2005. - № 2. - S. 39-42.
3. Podzolkova N.M. Effectiveness of ART programs using follitropin -  $\beta$  and ganireliks / N. M. Podzolkova, M. B. Anshina, J. A. Koloda and others. // Problems of reproduction. - 2008. - № 5. - S. 40-43.
4. Savelieva G.M., Laparoscopic surgery in gynecology: controversial issues. // In the book: Modern technologies in diagnosis and treatment of gynecological diseases: The material of scientific publications. Ed. Kulakov V.I., Adamian L.V. M: PANTORI, 2004. - P. 33-34;
5. Grienmehr E. Follitropin –  $\beta$  administered by pen device has superior local tolerance compared with follitropin –  $\alpha$  administered by conventional syringe / E. Grienmehr E., P. M. Bontje, Hoomans et al. // RBM Online 2001. № 3. P. 185 – 189.
6. Pasqualotto E. B. Effect of oxidative stress in follicular fluid on the outcome of assisted reproductive procedures / E. B. Pasqualotto, A. Agarwal, R. K. Sharma, et al.// Fertil. Steril. 2004. V. 81. P. 973-976
7. Peter Y.K. Prospective analysis of the relationship between the ovarian follicle cohort and basal FSH concentration, the inhibin response to exogenous FSH and ovarian follicle number at different stages of the normal menstrual cycle and after pituitary down-regulation / Y.K. Peter Young, T. David Barid, K. Joo Thong et al. // Hum. Reprod. 2003. № 18. P. 35 – 44.
8. Rodrigues R. In vitro modulation of FSH receptor by testosterone: a rationale for low

responders / R. Rodrigues, A. Pacheco, M. Martinez et al.// Hum Reprod. 2008. № 23. Suppl 1. Abstract Book. 491. P. 197.

---

**Slizovsky G.V., Maslikov V. M., Gjunter V. E.,**

**Titov M. V., Kuzhelivskij I.I.**

**Way of surgical correction of funneled deformation  
of thorax in children with use of nickelid  
titanium materials**

**GOU VPO "SibGMU" Roszdrav, sgv5858@mail.ru**

**Summary**

Congenital chest distortions are the defects associated with changes in the chest shape. Funnel chest (FC) is the most common. [1, 3]. Besides cosmetic defect this malformation is accompanied by cardiovascular and bronchopulmonary functional disorders. According to Russian authors 0.06 - 2.3% of children have FC, 0.2 - 1.3% according to foreign authors [6, 10, 11].

Surgical treatment of congenital chest distortions in children is one of the most serious and urgent problems of childhood thoracic surgery. Currently, there are many methods of thoracoplasty in children with congenital deformities [5, 7, 9]. Improvement and widespread implementation of minimally invasive high-tech methods in surgical treatment of congenital chest distortions is a great stride in this direction [4, 8]. However, some vital questions associated with selection of the optimal method for treatment remain unresolved, i.e. methods of thoracoplasty and sternocostal complex fixation.

**Work objective.** To estimate the titanium nickelide use efficiency in the surgical treatment of funnel chest.

**Materials and Methods**

Research is based on the analysis of 78 FC thoracoplastic operations performed at orthopedic department of MLPMU Children's City Hospital No. 4.

72 male and 6 female patients aged 4-20 years were operated over the 1977 to 2009 period. Clinical material is divided into 3 study groups according to the method of surgical treatment.