Puncture of ovarian follicles and ovarian endometrial in an in vitro fertilization program
In the past, the method used to obtain the follicular contents was puncture implemented during laparoscopy, effectively used in the 80-ies and 90-ies of the previous century. The introduction of transvaginal probe in gynaecologic ultrasonography has revolutionized the method of puncture of ovarian follicles. During the past 20 years collecting the egg cell under transvaginal ultrasound control (USG-TV) has become the standard method. This made it possible to increase the safety and efficacy in comparison with previously used laparoscopic methods [1, 2].

Popularisation of this method has led to continuous improvement of shape of the needle for aspiration, potentially maximizing the probability of egg cell retrieval [3, 4]. As a result, the double lumen needle was introduced to minimize the possibility of leaving the oocyte within the follicle.

One channel is used for oocyte aspiration, and the other for injection of fluid into the bladder and its flushing. The theoretical benefit of the double lumen needle is that the additional flushing of fluid into the follicle maximizes the probability of obtaining an oocyte [5]. This concept has initially been supported by several non-randomized studies, which showed encouraging data with application of follicle flushing [6-8]. However, subsequent randomized studies did not confirm these results [9, 10].

Despite the limited data to support the routine use of flushing the follicle [12], it is still frequently practiced procedure in many IVF clinics. However, there remain concerns about the potential benefits of flushing, performance techniques and therapeutic effects of therapeutic cycle [13-15]. The purpose of this systematic review of the literature and the meta-analysis is a summary of available published, randomized controlled trials on the effects of follicle rising, obtaining an egg cell and other parameters of therapeutic cycle under IVF program.

Flushing the follicle – simple aspiration

Levy et al, in a large meta-analysis published in the „Human Reproduction” did not show the prevalence of follicle flushing technique over simple follicle aspiration. [15] Both techniques provided similar number of oocytes retrieved and the performance of the procedures. These results were consistent in all six randomized clinical studies, which were subject to analysis.

Flushing the follicles involves longer duration of treatment, which in theory could lead to a slight increase in costs and risks of the procedure, although there are no data for a more detailed description of the problem [16]. The most extensive group was analysed by Haydardedeoglu et al (2011) - 518 cycles of IVF, while earlier work included 164 cycles (17). The materials developed did not show any difference in the effectiveness of IVF treatment between the group with follicle flushing and the group without follicle flushing.

These results differ from several non-randomized studies, which suggested that flushing the follicle increases the efficiency of procedures for egg cell obtaining [5]. However, they have in their design potential methodological errors, which may have influenced the results. In all three studies, each of these patients has been subjected to flushing the follicle and the control group was not created. Each of the follicles was punctured once and then the aspiration and flushing was made.

It was considered that oocytes obtained at the beginning are the result of direct aspiration, and oocytes obtained later on – of flushing. It is possible that oocytes classified to flushing phase were contained in the needle after aspiration and originated in fact from the first phase of procedure, even though they were assigned to follicle flushing phase. Some of studies carried out in the past, tried to address this issue by classifying the residue of oocytes obtained in the first flushing to cells derived from simple aspiration. Randomization of patients to flushing vs no flushing is the best method of comparing these techniques and solving the issue of improper assignment of oocytes to each of them.

In theory, increasing the efficiency of oocyte retrieval should lead to an increase in the number of embryos available for transfer, potentially increasing the likelihood of live birth. In the analysis of more than 400 000 IVF cycles Sunka-ra et al [15] showed that the probability of live births after applying IVF techniques signifi-
cantly increases in the event in which the total number of oocytes obtained increases from 1 to 10. Similar increase is no longer observed at higher number of oocytes, and in case of obtaining 15-30 oocytes the probability of live births remained at similar level.

Based on these data it can be concluded that in correctly responding patients we can expect no great advantage of follicle flushing because obtaining one or two additional oocytes does not improve the results significantly. However, women in whom the number of available oocytes is limited, can be a group in which the follicle flushing shall be potentially beneficial. The women belonging to this group are, among others, women poorly responding to therapy, women in the IVF program in natural cycles and those that received the minimum stimulation [12-14].

In one randomized controlled trial that evaluated the patients poorly responding to therapy, Levens et al observed no significant differences between the groups, and demonstrated classified insignificantly better quality of oocytes and their higher number in the group collected during flushing the follicles. However, this study was limited by the small number of attempts, i.e. 30 patients. A systematic review did not show any control data with randomization estimating the follicle flushing in IVF program in natural cycle or with minimal stimulation [11].

### Endometrial cysts in patients with infertility

Another issue emerging in terms of follicular puncture is the presence of endometrial cysts in patients with infertility problems. Including to the program the stimulation with exogenous gonadotropins in program of IVF patients with endometriosis is associated with the possibility of obtaining a smaller number of oocytes, a need to use higher doses of drugs and lower the concentrations of estradiol on the day of human chorionic gonadotropin (hCG) administration. However, data on the quality of the embryos obtained in patients with endometriosis in the literature are inconclusive. Recent studies on large groups of patients showed no significant difference between the quality of obtained embryos and the percentage of pregnancies after assisted reproduction treatment techniques in the groups of patients with endometriosis and ovarian factor related infertility. Thus, postulated in most publications less effective infertility treatment may be caused by improper selection of treatment group, in which there is a worse response to stimulation, resulting in a smaller number of obtained oocytes, their poorer quality and the negative effect on endometrium during the period of implantation window.

An alternative to the start of ovarian stimulation in IVF program is surgical treatment of cyst enucleation. Such conduct does not raise any doubts in case of large size changes (more than 5 cm in diameter). The enucleation of smaller changes has its supporters and opponents.

The removal of the changes prior to stimulation is suggested by the above mentioned effects of joining IVD program with endometriosis. Opponents postulate that surgical treatment can have the effect of reducing ovarian reserve, which in turn can lead to lower respond to stimulation of ovulation. Furthermore, implementation of treatment associated with surgery postpones the decision on treatment with IVF method even by up to six months. For young women, this is more recommended proceedings than in case of women, in which endometriosis was diagnosed at the age of about 40 years. In such cases, it is proposed to join immediately IVF program, in the absence of effective treatment in the first cycle the respond of the patient to stimulation and the course of embryonic development should be analyzed thoroughly. If these parameters do not diverge from standards for patients at this age, it is possible to consider joining the program again without surgery. In a situation of worse response to stimulation and lower number of embryos with unsatisfactory morphology, it is recommended to enucleate the endometrial cyst before next treatment program with use of assisted reproductive techniques.

In cases of joining the subsequent programs with use of assisted reproductive techniques by the patient with recurrent ovarian endometrial cysts it is possible to aspire the cyst contents during follicles puncture. However, this is done only after aspiration of the liquid from all the follicles. This procedure allows to avoid the toxic effects of the substances contained in endometrial cysts on the egg cell. This procedure is not generally as recommended due to technical difficulties during the aspiration of „thick“ contents of the cyst and the presence of strong pain after the puncture and the risk of infection. Alternative to this procedure is to perform aspiration of cysts in the months preceding the stimulation with use of gonadotropins with application of pituitary gland desensitization with gonadotropin releasing hormone – GnRH. Such action makes it easier to carry out the procedure (smaller, more accessible ovary, less „thick“ content of the cyst and the subsequent inclusion of stimulation in patient “without cyst”.

In younger patients, it is recommended to enucleate the endometrial cyst prior to IVF program joining. In case of stating minor endometriosis during diagnostic laparoscopy it is recommended to coagulate them, which involves small but statistically significant increase in fertility.
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Literature:


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