Intrauterine insemination – current indications

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Abstract
In spite of the vast use of highly advanced and effective methods of assisted reproductive technology i.e. in vitro fertilization and embryo transfer (IVF-ET) with intracytoplasmic sperm injection (ICSI), the intrauterine insemination (IUI) procedure has its own indications and place in treating infertility. The popularity of the IUI results from the fact that it is a relatively simple procedure and the cost of treatment is lower compared with IVF. The rate of achieved pregnancies per cycle with IUI is the highest among couples with unexplained infertility and the lowest among couples in whom there is a number of factors limiting fertility determined. Potentially, the effectiveness of artificial insemination is influenced by many factors, i.e. indications: the appropriate choice of the treated couple, the duration of infertility, woman’s age, semen quality, semen preparation, the number of inseminations in a cycle, mild ovarian hyperstimulation, the number of inseminations that a couple has already undergone. However, the discussion concerning the role of insemination in treating male factor infertility, especially less severe, is still open and the necessity of well-planned research, in which the insemination effectiveness would be measured by the percentage of live births is emphasized.

Key words: infertility, assisted reproductive technologies, intrauterine insemination

The history of intrauterine insemination (IUI) goes back to the 18th century when Scottish surgeon John Hunter performed an effective procedure with the use of the husband’s sperm. In 1884, after William Pankhurst from Philadelphia in the United States applied the donor’s sperm [1, 2], the live birth was reported.

There are still ongoing discussions about the role of intrauterine insemination in the era of assisted reproductive technology i.e. IVF/ICSI.

The clinical task for the doctor in charge is to conduct the diagnostic process in such a way that the optimal infertility treatment is proposed with full awareness, with the participation of the treated couple and in the shortest possible time [3, 4].

The recommendations prepared by the expert bodies are to help clinicians as well as patients in making an optimal decision concerning the methods of treatment and the safety of the procedures used. They should also support a clinician, which has been emphasized lately, in seeking the balance between the cost of therapies and their effectiveness [5].

As the statistical data show, the insemination is still a popular method of treatment – according to European Society of Human Reproduction and Embriology (ESRHE) in 2009 in Europe 162,843 IUI-H cycles were performed compared with 135,621 cycles of IVF procedures carried out during the same time [6].

The popularity of the IUI results from the fact that it is a relatively simple procedure and the cost of treatment is lower compared with IVF. In the case of IUI, the time of stimulation is shorter and therefore the stimulation itself is cheaper as well as the monitoring of ovulation procedure. It is not without significance that a doctor can learn the procedure in quite a short time.

In countries where the access to IVF/ICSI is significantly limited by e.g. the lack of even partial coverage of costs, insemination treatment remains an important therapeutic step that can be offered to a couple who is unsuccessfully trying to have a child.

However, although the IUI is undeniably a cheaper method of infertility treatment and less stressful for patients and medical staff, it needs to be emphasized that the most effective form of treating infertility is still IVF. The place of IVF/ICSI remains undoubtedly fundamental in case of bilateral fallopian tubes obstruction, severe male factor or serious ovulation disorders [3].

The ESHRE data indicate that the pregnancy rate per cycle (PR per cycle) after IUI-H is 12.4% compared with 28.9% after IVF and the results have not changed over the last few years [7].

According to ESHRE experts IUI combined with the ovulation stimulation before the IVF treatment trial can be offered to the infertile couples because of low cost of procedure and potential success in the form of preg-
nancies in numerous couples qualified for such a treatment [3].

The rate of achieved pregnancies per cycle with IUI is the highest among couples with unexplained infertility and the lowest among couples in whom there is a number of factors limiting fertility determined [8].

The term artificial insemination (AI) includes a lot of techniques. The insemination can be intravaginal, intracervical, intrafallopian, intraperitoneal. However, in the clinical practice the intrauterine insemination is most often performed. Its effectiveness in the form of live births outnumbers other methods of insemination [9].

Potentially, the effectiveness of artificial insemination is influenced by many factors, i.e. indications: the appropriate choice of the treated couple, the duration of infertility, woman’s age, semen quality, semen preparation, the number of inseminations in a cycle, mild ovarian hyperstimulation, the number of inseminations that a couple has already undergone [10].

According to the retrospective analysis of the factors contributing to the conception in the cycle with the intrauterine insemination, the couple that has high potential of achieving pregnancy is characterized as the following: woman – aged under 30 with the infertility factor – intracervical or the lack of ovulation whereas man – in whom total motile spermatozoa TMS \( \geq 5 \) million; in the stimulated cycle the two follicles larger than 16 mm were achieved, the estradiol concentration on the day of applying human chorionic gonadotropin hCG is \( >500 \) pg/ml and the procedure is conducted with the use of a soft catheter [11].

The development of the semen preparation technique for IVF i.e. wash, swim-up, swim-down or the use of density gradients contributed also to the fact that in the era of IVF/ICSI the insemination procedure has not been totally supplanted. There is no evidence, however, that there is one method of semen preparation technique which would contribute to the increase of clinical success in the form of pregnancies after IUI [3, 12].

The obvious indication for the artificial insemination is the need to use donor insemination.

Such a kind of procedure is suggested for couples in whom the man is a carrier of a genetic mutation or inherited disorder with high potential of transmitting it to the offspring such as Huntington’s disease or hemophilia [1].

Unsuccessful attempts with the use of the husband’s semen in IVF or ICSI and couples in whom the IVF procedure cannot be proposed (e.g. financial barrier) and the presence of severe oligoasthenoteratozoospermia or obstructive or non-obstructive azoospermia which do not give chance for pregnancy are also factors that qualify to IUI with the donor’s semen [1, 13].

If there is a high risk of transmitting an infectious disease to the recipients by the partner or there is a severe Rhesus incompatibility of the mother then the donor insemination should be also considered.

In some countries the donor insemination is allowed in the case of homosexual couples and single women who want to have a baby [1, 13].

There is no final consensus concerning the semen parameters which should qualify for ICSI rather than IUI. This results from various criteria used in publications – some take into account the semen parameters before, others after preparation. The latest metaanalysis of the above publications states that the cut-off value for TMS count for semen before preparation is 5-10 million and in the range of total motility – 30%. In the case of the semen after preparation cut-off value for the number of TMS count is between 0.8-5 million, and for sperm morphology using strict criteria is \( \geq 5\% \) normal morphology [15].

In the case of sexual disorders such as erectile dysfunctions, ejaculatory failure, vaginismus and also hypospadias – infertility treatment with IUI can be used [1, 2]. However, there are voices that this is unnecessary due to the fact that in the case of these pathologies the possibility of depositing the semen near the cervix occurs. On the other hand, the use of IUI is justified in the case of premature ejaculation (organic, iatrogenic), which is often accompanied by reduced semen parameters. In such situations the proper method of obtaining sperm – from centrifuged and previously alkalinized urine – allows it to be used for IUI, IVF or ICSI [1, 2, 4].

The indications for IUI in case of male-factor infertility are based on the assumption of increasing the chance for conception by placing selected, the most motile sperm near the egg cell, omitting the way through the vagina adverse environment and not always sperm-friendly cervical mucus.

In the case of less severe forms of male-factor infertility, one of the publications confirms the effectiveness of gonadotropin stimulation in achieving pregnancy, yet, in the case of severe deviations of semen parameters such effectiveness has not been confirmed [15, 16].

The analysis published in Cochrane database concerning the effectiveness of the use of IUI in the case of male subfertility with stimulation or without ovulation in
In comparison with timed intercourse (TI) did not indicate higher effectiveness of the procedure in achieving pregnancy [17].

However, the discussion concerning the role of insemination in treating male factor, especially less severe, is still open and the necessity of well-planned research, in which the insemination effectiveness would be measured by the percentage of live births is emphasized [4].

In the case of the isolated cervical factor (defined as a negative post-coital test, normal semen parameters and the adequate timing of an intercourse), the significant increase of the chance for pregnancy with the use of IUI in the non-stimulated cycle has been stated [18].

The endometriosis is a common indication for IUI insemination. According to many authors, it can be offered as a method of treating women before the age of 38 and with 1st and 2nd stage of endometriosis according to AFS [19].

The use of stimulation in the preparatory process for IUI undoubtedly has its advantages. It triggers an increase of oocytes available for fertilization, provides the possibility to plan the most appropriate moment of application, and finally allows overcoming some minor endocrine disorders and at the same time optimizes the process of ovulation.

The disadvantages of stimulation are the increase of the risk of multiple pregnancies and the ovarian hyper-stimulation syndrome [3, 4, 10]. Therefore, what is important in these cases is to monitor the cycle, have experienced doctors in charge and determine strict cancellation criteria [10].

The stimulation should be used in subfertile couples – the effectiveness of the insemination with ovulation stimulation in couples with unexplained infertility was confirmed in randomized surveys [20]. The ovulation stimulation combined with IUI, however, does not increase the percentage of pregnancies in the case of the cervical and male factor [10].

The intrauterine insemination without drug stimulation should be considered as an option of treatment in couples: 1) who are not able or have great difficulties in having sexual intercourse due to the clinically diagnosed disability or the psycho-sexual problems, 2) who need special methods of conception (e.g. sperm washing if the partner is HIV-positive) and people of the same sexual orientation [13]. To sum up, the intrauterine insemination is a cost-effective and efficacious procedure in some group of patients [10].

In spite of the vast use of highly advanced and effective methods of assisted reproductive technology i.e. IVF/ICSI, the IUI procedure has its own indications and place in treating infertility.

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