PREGNANCY AFTER CERVICAL CONIZATION – A LITERATURE REVIEW

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ABSTRACT

Cervical intraepithelial neoplasia (CIN) is a precancerous stage of cervical cancer, one of the most easily preventable cancers in women. It is treated with conization, a procedure that can be performed using various methods. Because CIN is often diagnosed in women of reproductive age, there is a strong need to study the consequences of conization for patients planning future pregnancies. According to different studies, this procedure may result in adverse pregnancy outcomes such as preterm delivery, low birth weight and increased perinatal mortality. Many factors can influence these complications, including a particular method of conization, the size of the lesion and a woman's previous obstetric history. Subfertility is yet another, often researched potential complication of conization. Regardless of the extent of complications, it is proven that conization does influence future pregnancies, thus a careful clinical approach for patients with a history of this procedure is required.

BACKGROUND

Cervical cancer remains one of the most common gynaecological neoplasms worldwide with over half a million new cases diagnosed each year [1]. About 90% of deaths from cervical cancer occur in the developing countries, where an adequate comprehensive approach in a form of prevention, effective screening, early diagnosis and treatment programs is not fully developed [2]. However, a graduate introduction of these measures in many parts of the world has allowed to significantly decrease both the incidence and mortality from cervical cancer in the last decades [3].

Pap smear is one of the factors which has contributed to reducing the incidence of cervical cancer, being the basic method for cervical screening by detection of cervical precancerous or cancerous lesions, known as cervical intraepithelial neoplasia (CIN). Those abnormalities are usually treated with conization, which can be either a diagnostic or a therapeutic procedure performed in a form of cold knife conization (CKC), large loop excision of the transformation zone (LLETZ) also known as loop electrosurgical excision procedure (LEEP) or laser conization. Besides conization, other methods include ablative procedures, such as laser ablation, cryotherapy, cold coagulation and diathermy [4, 5]. Given the fact that the average woman who is diagnosed with and treated for CIN is around 30 years old, it is important to take into consideration the possibility of future pregnancy [5]. Many studies suggest that women treated for CIN have a higher risk of adverse pregnancy outcomes, including risk of preterm birth, low birth weight and premature rupture of membranes [6, 7]. Moreover, there are various reports that the treatment of CIN may also influence women's ability to conceive [6]. Therefore, it is especially important to analyse and assess short- and long-term consequences of various therapeutic methods of cervical intraepithelial neoplasia considering an increasing number of women who want to conceive in their 30s.

PREGNANCY COMPLICATIONS

There is an association between cervical intraepithelial neoplasia treatment and increased risk of adverse obstetric outcomes. In this review we would like to focus on conditions such as perinatal mortality, low birth weight and preterm delivery in future pregnancies [8, 9]. The cause of these complications stays unclear. However, potential underlying reasons include anatomical changes, cervical scarring, changes in the innate immune system or in cervicovaginal flora as well as simple lack of mechanical support [6, 8]. Castanon and colleagues indicated in their study that the increased risk of adverse obstetric sequelae may not be a result only of the treatment itself, but it may be associated with common risk factors which predispose to precancerous cervical conditions [8]. Nevertheless, there is no certain evidence which testifies the exact pathogenesis of adverse pregnancy outcomes in this group of patients.

Recent meta-analyses showed that there is a strong association between preterm delivery and history of CIN treatment [9, 10]. This association differs depending on the treatment technique and is most evident for cold knife excision, followed by laser conization, large loop excision of the transformation zone and lastly, laser ablation [7, 8, 9].

The impact on preterm birth is stronger at earlier gestational ages and rises with the amount of excised tissue [7]. A Danish study revealed that increasing cone depth was positively associated with increased risk of preterm delivery [11]. In a recent U.K. study, the risk of preterm delivery was minimally affected by small excisions, whereas larger excisions were followed by doubled risk, which suggests that the morphology of the lesion is another vital determinate [12]. Moreover, the risk becomes gradually less significant with every year after treatment [7].

The next important and quite common condition which may develop after cervical conization is low birth weight. The studies show that the incidence of birth weight <2500 g is significantly higher for women treated with cold knife conization, large loop excision of the transformation zone, laser conization and less for ablative treatment [9, 10].

There are some reports that cold knife conization and excisional treatment were associated with extreme low birth weight under 1000 g whereas laser ablation seem to be free of these complications [9].

Treatment of cervical intraepithelial neoplasia may also lead to miscarriages. Although the frequency of total miscarriages as well as miscarriages in the first trimester of the pregnancy was quite similar for women after conization and in the control group, cervical treatment increased the risk of miscarriage in the second trimester. This association is the strongest in case of laser conization, loop electrosurgical excision procedure and cold knife conization [6, 9]. Treatment with diathermy also increases the risk of perinatal mortality. Nevertheless, ablative treatment seems to be safe in this aspect [9].

Some studies show that there was also higher rate of ectopic pregnancies among treated women [13].

FERTILITY

Whereas the influence of CIN treatment on obstetric outcomes has been extensively described, there are still limited data on the conization influence on the ability to conceive, often contradictory and poorly documented. Among underlying mechanisms which may influence women's fertility after conization we can distinguish removal of a part of the endocervical canal, followed by decreasing the number of the mucus-secreting endocervical glands and, in result, a smaller amount of secretions which facilitate penetration of the sperm and conception. Another possible reason constitutes the healing process after excision, which may result in structural changes of the cervix and can be associated with the loss of normal cervical function. It can also be a cause of severe stenosis of the cervical opening, which may further prevent penetration of the sperm and conception [6, 13].

Nevertheless, the recent research indicates that there is no evidence suggesting that the cervical intraepithelial neoplasia treatment may adversely affect the ability of

conception . Two studies showed that there is no significant difference in the pregnancy rate in women with an intention to conceive comparing patients with and without history of conization [13, 20]. The recent meta-analysis also revealed that both groups of women did not differ considerably [6].

The other outcome which was taken into account in some studies included the time needed to conceive. The results differed depending on the study, some of them reported that there is no significant difference, however, another one shows that the percentage of women who required more than one year to conceive was considerably higher among women after conization, regardless of the method [14].

DISCUSSION

Cervical intraepithelial neoplasia is a quite common condition, also among women in the reproductive age. Thus, a proposed method of treatment should not only include factors such as invasiveness of the treatment or the time of recovery, but also possibility and potential consequences for pregnancy.

Clinically significant risk of preterm birth is one of the most common complications after conization mentioned in various studies, especially in early gestational age groups [17]. Women without previous preterm birth are even more predisposed to experience this condition after conization. The risk logically increases after repeat procedures, requiring a careful clinical approach during the selection of patients for the procedures, especially with a recurring condition [18].

Although cervical neoplasia should not be strictly associated with women's laxity, there are however some certain elements of lifestyle that are risk factors for the development of CIN, including early age of first intercourse, number of sexual partners and statistically higher risk of genital infections. Thus, for women from such risk groups, it is difficult to determine the exact genesis of the complications, i.e. extrauterine pregnancy, as they can result from earlier genital infections [13].

Regarding the fertility studies we cannot draw clear conclusions to which extent the longer time to pregnancy is a result of conization and to which is the consequence of a doctor's recommendation to refrain from conception during early postoperative period and until any residual diseases is ruled out in the next follow-up assessment [6]. Regardless, methods of treatment including the destruction of mucus-secreting glands may lead to unwanted longer time to pregnancy [6].

One of the limitations of most studies is the lack of differentiation between smokers and non-smokers. It is documented that there is a bigger proportion of smokers among patients with CIN than in the general population [15]. Therefore, the incidence of pregnancy may seem smaller because of the smoking population. Adequately, potential cessation of smoking after the treatment could also change the results [13].

CONCLUSION

Selection of a particular method of conization should be an individual approach based on the age of the patient, medical history and CIN excessiveness. Women, especially those for whom pregnancy after conization is their first one, should be extensively informed about possible adverse pregnancy outcomes following the procedure. Watchful observation and solid perinatal care is an effective method of early detection of potential pregnancy complications after conization.

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ABBREVIATIONS

CIN – cervical intraepithelial neoplasia
CKC – cold knife conization
LEEP – loop electrosurgical excision procedure
LLETZ – large loop excision of the transformation zone

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