Vpliv kajenja na pogostnost in značilnosti zapletov po konizaciji z diatermijsko zanko (LLETZ)

The influence of smoking on the frequency and characteristics of complications following large loop excision of the transformation zone (LLETZ)

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Izvleček

Namen: *Ekscizija transformacijske cone z zanko (LLETZ) je metoda izbora za zdravljenje žensk s potrjeno intraepitelno cervikalno lezijo ali s sumom nanjo. Glede na spoznanja o tem, da kajenje zavira celjenje ran, smo želeli izvedeti, ali kajenje povečuje incidence najbolj pogostih zapletov po LLETZ posegu in kako vpliva na njihovo jakost in trajanje.*

Metode: *V raziskavo smo vključili 434 bolnic, pri katerih smo v letih od 1993 do 2015 na Kliniki za ginekologijo in perinatologijo Univerzitetnega kliničnega centra Maribor naredili LLETZ. Pooperativno so bolnice izpoljevale vprašalnik, v katerem so ocenjevale trajanje in intenziteto bolečin v spodnjem delu trebuha, krvavitve iz nožnice in izcedka iz nožnice. Tako dobljene podatke smo analizirali.*

Abstract

Purpose*: Large loop excision of the transformation zone (LLETZ) is the procedure of choice for treating patients with suspected or confirmed cervical intraepithelial lesions. Since it has been established that smoking impairs wound healing, we wanted to determine if smoking increases the incidence of the most common complications that follow the LLETZ procedure and how it affects their intensity and duration.*

Methods: *We included 434 patients that underwent the LLETZ procedure between 1993 and 2015 in the Department of Gynecology and Perinatology, University Medical Centre Maribor. Patients were asked to assess the intensity and duration of abdominal pain, vaginal bleeding and vaginal discharge after the procedure, and to complete a questionnaire on a daily basis. Data ob-*

Rezultati: *V skupini je bilo 237 (54,6 %) kadilk in 197 (45,4 %) nekadilk. Po LLETZ je 237 bolnic (54,6 %) poročalo o izcedku iz nožnice, 193 (44,5 %) jih je imelo bolečine v spodnjem delu trebuha, 181 (41,7 %) pa jih je krvavelo. Pojavnost posameznega zapleta med kadilkami in nekadilkami se ni značilno razlikovala, tudi trajanje in jakost izcedka in bolečin ne, več nekadilk kot kadilk je krvavitev opisalo kot močno.*

Zaključek: *Glede na rezultate naše raziskave kajenje ne povečuje incidence pooperativne vaginalne krvavitve, bolečin v spodnjem delu trebuha in vaginalnega izcedka po LLETZ. Bistveno tudi ne vpliva na njihove značilnosti in trajanje.*

tained from the questionnaires were then analysed.

Results: *The study group consisted of 237 (54.6%) smokers and 197 (45.4%) non-smokers. After the LLETZ procedure, 237 (54.6%) patients noted the occurrence of vaginal discharge, 193 (44.5%) lower abdominal pain, and 181 (41.7%) vaginal bleeding. No significant difference was observed in terms of the incidence of the observed events when comparing smokers and non-smokers. The duration and intensity of vaginal discharge and pain were not significantly different between the two groups. Non-smokers experienced bleeding that was more severe than smokers.*

Conclusions: *According to the results of our study, smoking did not increase the incidence of vaginal bleeding, vaginal discharge, and lower abdominal pain following the LLETZ procedure, nor did it crucially influence their duration and intensity.*

INTRODUCTION

Large loop excision of the transformation zone (LLETZ) is the preferred procedure when cervical intraepithelial neoplasia (CIN) is suspected or confirmed (1, 2). LLETZ is a form of excisional treatment (Figure 1, 2). When compared to cold-knife conisation, LLETZ is faster, with less intraoperative bleeding and a shorter hospital stay (3). The regeneration process in the uterine cervix after LLETZ depends upon the proportion of the excised volume and remaining cervical tissue and appears to be completed within 6 months (4, 5). Wound healing is a well-regulated process that includes several phases. In physiological circumstances, this process results in wound closure within several days or weeks (6). Smoking interferes with the process of healing by causing delays that occur through numerous mechanisms, including decreased tissue oxygenation and aerobic metabolism, reduced inflammatory cell chemo-tactic responsiveness, migratory function and oxidative bactericidal mechanisms, reduced fibroblast proliferation and the down-regulation of collagen synthesis and deposition (7).

Although LLETZ appears to be uncomplicated and an efficient procedure under local anaesthesia, some peri- or postoperative complications may follow (2, 8-11). Most complications are minor and short-term, including secondary vaginal bleeding, lower abdominal pain and secondary infection with consequent vaginal discharge (1, 8, 12-14).

The aim of our study was to determine whether the healing process after LLETZ can be influenced by a patient's smoking status.

MATERIALS AND METHODS

This retrospective study involved 434 patients who had been treated with the LLETZ procedure between 1993 and 2015 at the University Medical Centre Maribor. CIN lesions were the most common indicators for LLETZ in our study.

All women underwent a detailed interview before LLETZ was performed. Historical data were collected via a standard questionnaire. Smoking status was defined by current smoking habits. Following the procedure, patients were asked to monitor the occurrence of pain, vaginal discharge or vaginal bleeding for the next 90 days. They were also asked to evaluate

the intensity of these symptoms on scale from 0 to 3 (0 meaning no complication and 3 meaning severe symptoms).

Statistical analysis

We used the x^2 test to compare the occurrence of postoperative symptoms between smokers and non-smokers, and the Student's t-test to evaluate quantitative parameters. A $p < 0.05$ was considered statistically significant.

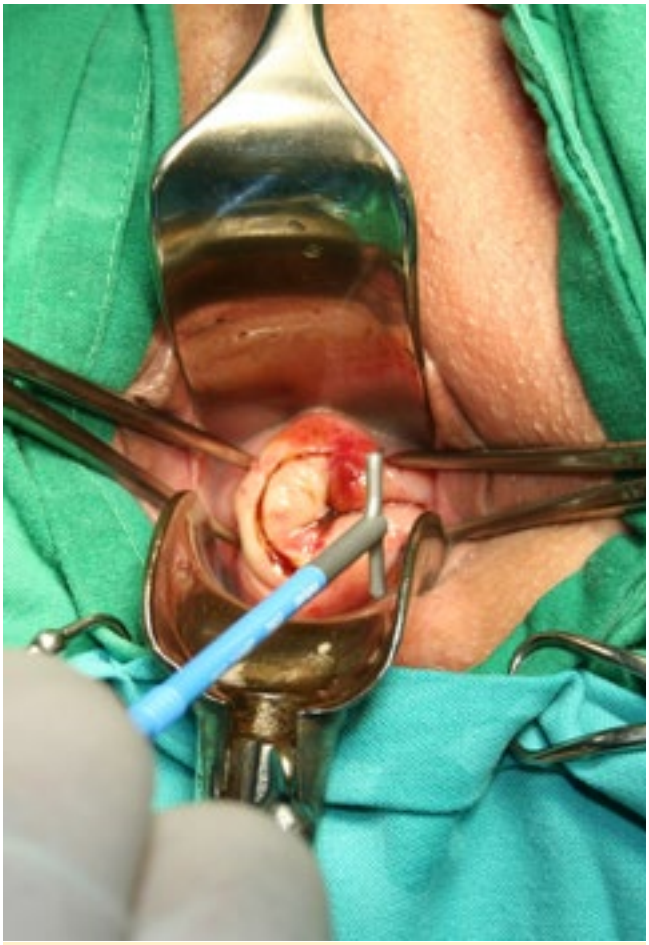

Figure 1. *Large loop excision of transformation zone (LLETZ)*

RESULTS

Of the 434 patients who underwent the LLETZ procedure, there were 237 (54.6%) smokers and 197 (45.4%) non-smokers. CIN was the indicator for LLETZ in 397 patients (91.5%). Others had the procedure because of repeatedly suspicious cervical smears. The median age of smokers was 32.6 ± 7.8 years, while that of the non-smokers was 34.27 ± 8.8 years.

Figure 2. *Cervix immediately after large loop excision of transformation zone (LLETZ)*

Vaginal discharge was reported by 237 patients (54.6%), lower abdominal pain by 193 patients (44.5%), and vaginal bleeding by 181 (41.7%) patients. The frequencies of each complication were compared between the two groups of women (smokers and non-smokers) by the x^2 test. No statistically significant differences were found between the groups (Table 1). Comparisons of the durations of each complication between the two groups showed no statistically significant difference in terms of the duration of pain, vaginal discharge, or postoperative bleeding (Table 2).

On average, the intensity of complications was mild. On a scale from 0 to 3, the mean intensity of lower

abdominal pain was 0.61, of vaginal discharge was 0.72, and the intensity of vaginal bleeding was 0.50. Grade 3 pain was experienced by only 2.5% of the entire study group. Grade 3 vaginal discharge and bleeding were experienced by 3.6% and 3.9% of patients, respectively. Comparisons of the intensities of lower abdominal pain and vaginal discharge showed no statistically significant differences in terms of smoking status. The intensity of bleeding was higher in non-smokers (Table 3).

Table 1: *Comparison of incidence of complications after LLETZ between smokers and non-smokers*

Symptom	Smokers (N = 237)	Non-smokers (N = 197)	p
Pain	101 (42.6%)	92 (46.7%)	0.390
Vaginal discharge	127 (53.8%)	109 (55.3%)	0.716
Bleeding	91 (38.4%)	90 (45.7%)	0.125

Table 2: *Duration of pain, vaginal discharge and bleeding after LLETZ (days ± SD) in smokers and non-smokers*

Symptom	Smokers	Non-smokers	p
Pain	7.35 ± 17,11	5.73 ± 9,01	NS
Vaginal discharge	15. 93 ± 30.57	16.87 ± 24.19	NS
Bleeding	5.09 ± 10.33	5.69 ± 9.74	NS

Table 3: *Intensity of pain, vaginal discharge and bleeding after LLETZ in smokers and non-smokers*

Symptom	Smokers	Non-smokers	p
Pain	0.55 ± 0.84	0.67 ± 0.87	NS
Vaginal discharge	0.68 ± 0.89	0.75 ± 0.94	NS
Bleeding	0.38 ± 0.71	0.61 ± 0.95	$p < 0.05$

DISCUSSION

Excision of the transformation zone leaves a raw area on the cervix that can lead to infection after the procedure. The incidence of infection following LLETZ is low, between 0.8 and 14.4%, but would probably be much higher if delayed bleeding and vaginal discharge are also included (15).

More than half of our patients reported no complications after the LLETZ procedure, and only 2 – 4 % of women experienced severe complications. This is in accordance with other studies, which found that the LLETZ procedure was safe and reliable (10, 11, 13, 16). The evaluation of complications in our study was graded by the patients themselves, which has the disadvantage of being subjective. Vaginal discharge, vaginal bleeding, and lower abdominal pain after the procedure should be distinguished from regular menstruation, which women were instructed to mark separately in their notes. This could have led to some false results in our data, considering that some of the patients did not acknowledge this or distinguish complications from their menstrual period.

Prolonged vaginal discharge after LLETZ is not necessarily caused by infection. It can also appear due to the healing process or local oedema. According to Chamot et al., some form of vaginal discharge was noted by virtually all women (79% to 100%), with a duration of 14 ± 4.6 days (17). The duration of vaginal discharge was similar in our patients, but occurred less frequently, since it was observed by 54.6% of patients and lasted for 15.93 ± 30.57 days in smokers and 16.87 ± 24.19 days in non-

smokers. Lower abdominal pain was experienced by 44.5% of our population with a duration of 5.7 days in non-smokers and 7.35 days in smokers. Such durations were longer than that reported by Adewole et al., who observed longer lasting pain or pain associated with the next menses in 67% of patients after LLETZ with a mean duration of 1-2 days (18). Delayed postoperative bleeding, lasting for 3 to 4 days on average, is common for uncomplicated LLETZ, since it is experienced by almost all women (17). In our study, only 41.7% of patients complained of vaginal bleeding, but it lasted longer (5 days in smokers and 5.67 days in non-smokers). The intensity of bleeding was higher in non-smokers. Six percent of non-smokers described their bleeding as grade 3, compared to only 2.1% of smokers. The association between the excision of more than 20 mm of tissue and a greater risk for vaginal bleeding and infection following LLETZ was previously confirmed by Kietpeerakool and Suthicon (2009) (13). Tobacco is a peripheral vasoconstrictor, and nicotine increases platelet adhesiveness, raising the risk of micro-vascular occlusion and tissue ischemia, which can cause a delay in healing (19). In their systematic review, Pluvy et al. showed that smokers had an increased risk for surgical site infection and delayed healing with cutaneous necrosis in plastic surgery operations, but did not report on the postoperative bleeding pattern with regards to smoking status (20).

The carcinogenic effect of smoking on the cervical mucosa has already been confirmed by many studies; smoking damages DNA, causes changes in cell proliferation and weakens the local immune response (21-26). Following infection with human papilloma viruses (HPV), the promotion of CIN progression has been associated with smoking (23, 26). Studies have showed that progression is dose-dependent and was increased for women who smoked 20 or more cigarettes per day (13, 26). Because of the known influence that smoking has on wound healing through many different mechanisms (7), we expected to find signs of impaired wound healing caused by LLETZ, such as pain, vaginal discharge, and bleeding. We failed to confirm any difference in the process of healing when comparing smokers to non-smokers in terms of the incidence of symptoms, their duration and the intensity of lower abdominal pain, and vaginal discharge. Bleeding was more intense in non-smokers. There appears to be no connection between genital pathogens, HIV infection, Chlamydia trachomatis infection, and post-LLETZ vaginal bleeding (13, 16, 28). Further studies should be conducted to define why some women experience up to 40 days of postoperative vaginal bleeding or discharge from the operating site, when in most cases, there is none or very little complication.

In conclusion, smokers have no greater risk for complications, such as a higher occurrence of vaginal bleeding, vaginal discharge, or lower abdominal pain following the LLETZ procedure. When one of these complications occurs, it is mostly mild and short-lasting.

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