Prospektivna raziskava povezave med okužbo maternične vratu in sekundarno krvavitvijo po eksciziji transformacijske cone z električno zanko (LLETZ)

A prospective study of the correlation between infection of the uterine cervix and secondary bleeding after large loop excision of the transformation zone (LLETZ)

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Izvleček

Namen: *Namen prospektivne raziskave je bil ugotoviti, ali okužba spolnega trakta s patogenimi mikroorganizmi vpliva na pojavljanje hude pooperativne krvavitve, ki zahteva sekundarni poseg po eksciziji transformacijske cone z električno zanko (LLETZ).*

Metode: *V raziskavo je bilo vključenih 1.419 bolnic s cervikalno intraepitelijsko neoplazijo (CIN), pri katerih smo opravili LLETZ. Pred posegom smo bolnicam odvzeli bris maternične vratu na patogene mikroorganizme. Po posegu smo pri bolnicah spremljali pojav hudih pooperativnih krvavitev, ki so zahtevale sekundarni poseg.*

Rezultati: *Patogeni mikroorganizmi so bili prisotni pri 714 (50,3 %) bolnicah in odsotni pri 705 (49,7 %) bolnicah. Najpogosteje izolirani patogeni mikroorganizmi so bili β–hemolitični streptokoki skupine B, α–hemolitični streptokoki, enterokoki in koliformne*

Abstract

Purpose: *A prospective study was undertaken to evaluate the role of genital pathogens in postoperative bleeding necessitating secondary intervention after large loop excision of the transformation zone (LLETZ) of the uterine cervix.*

Methods: *A total of 1419 patients with cervical intraepithelial neoplasia (CIN) who underwent LLETZ were included in the study. To determine the presence of genital pathogens, cervical swabs were collected before the procedure. Postoperatively, patients were followed up for bleeding necessitating secondary interventions.*

Results: *Among 1419 patients, genital pathogens were present in 714 (50.3%) cases and absent in 705 (49.7%) cases. The most frequently isolated groups of microorganisms were group–B β–haemolytic strepto-*

bakterije. Revizija zaradi hude pooperativne krvavitve je bila potrebna pri 48 (6,8 %) bolnicah brez patogenih mikroorganizmov in 63 (8,8 %) bolnicah s pozitivnimi brisi na patogene mikroorganizme. Razlika ni bila statistično značilna (hi–kvadrat = 1,72; P > 0,05).

Zaključek: *Bolnice s CIN imajo zelo pogosto prisotno okužbo maternične vratu s patogenimi mikroorganizmi. Ta okužba ni pomembno vzročno povezana s pojavom hude pooperativne krvavitve, ki zahteva sekundarni poseg po LLETZ.*

cocci, α–haemolytic streptococci, Enterococcus sp. and coliforms. Secondary procedures due to severe bleeding were required in 48 (6.8%) patients without and in 63 (8.8%) patients with genital pathogens, but this difference was not significant (chi–square test = 1.72; P>0.05).

Conclusion: *These data suggest that genital pathogens are very common in patients with CIN and are not an important cause of postoperative bleeding necessitating secondary intervention after LLETZ.*

INTRODUCTION

Large loop excision of the transformation zone (LLETZ) has been in use for more than two decades. It is now the first–line treatment for cervical intraepithelial neoplasia (CIN) (1–3). It provides reliable histological specimens and has comparatively low morbidity (4, 5). Secondary bleeding is known to be one of the most common adverse effects after this procedure (6–9). The association between bacterial infection of the lower genital tract and morbidity after abdominal hysterectomy is not disputed (10–12), but evidence suggesting a potential role of genital pathogens in bleeding after LLETZ is more scarce (13, 14). We previously found that bleeding after LLETZ does not occur more frequently in patients with infection with *Chlamydia trachomatis* (15).

The present study was designed to determine if the presence of genital pathogens influences the prevalence of severe postoperative bleeding necessitating secondary treatment after LLETZ.

Ethical approval of the study protocol

The study protocol was approved by the Ethics Committee of Maribor University Clinical Centre (Maribor, Slovenia). All patients provided written informed consent to be included in the study.

MATERIAL AND METHODS

A prospective study that lasted from January 1993 to December 2005 involved 1419 patients who underwent LLETZ at the University Clinical Department of Gynaecology and Perinatology (Maribor University Clinical Centre). The study involved women with CIN requiring LLETZ based on histological proof obtained by punch biopsy. All women underwent a standard gynaecological interview and pre–procedure counselling.

An endocervical smear was taken before the procedure to detect genital pathogens. Swabs were collected in Amies transport medium for inoculation onto culture media for subsequent isolation of anaerobes, streptococci groups A–G, coliforms, *Staphylococcus aureus*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Candida* species.

The surgical procedure was undertaken under local anaesthesia in an outpatient setting. LLETZ was carried out using an Elektrotom 400 Unit (Berchtold, Berlin, Germany) with loop devices ranging in size from 10 mm to 20 mm. The procedure was carried out using blended current with a cut frequency set to 40 W and a coagulation frequency set from 20 W to 40 W. The wound surface was electrocoagulated.
All specimens were fixed with 10% formalin, seri-

ally sectioned, and embedded in paraffin. They were processed overnight using standard techniques, and stained with haematoxylin and eosin.

Patients were asked to record, on a daily basis, bleeding they experienced in the first 90 days after the procedure. Secondary procedures (i.e., vaginal pack or sutures or both) were carried out due to excessive bleeding if deemed necessary. Three months after the procedure, patients returned for a follow–up visit. A gynaecological examination was done, a cervical smear taken, and information sheets with recorded postoperative bleeding collected at this time.

Statistical analyses

Using the χ^2 test, groups of patients with and without genital pathogens were analysed for significant differences in the occurrence of postoperative bleeding requiring a secondary procedure. $P<0.05$ was considered significant.

RESULTS

Secondary procedures due to severe bleeding were undertaken in 111 (7.8%) patients. The age and parity of patients with and without treatment due to secondary bleeding are shown in Table 1. The patients in both groups were of similar age and parity.

Genital pathogens were present in 714 (50.3%) and absent in 705 (49.7%) cases. The most frequently isolated groups of microorganisms were group–B β–haemolytic streptococci, α–haemolytic streptococci, *Enterococcus* sp. and coliforms. The frequency and type of secondary procedure due to post–LLETZ bleeding among patients with genital pathogens and those without genital pathogens are shown in Table 2. Secondary procedures were carried out in 63 (8.8%) patients with and 48 (6.8%) patients without genital pathogens. The difference was not significantly different (chi–square test = 1.72; $P>0.05$).

Table 1. *Age and parity of patients who did and did not need secondary procedures due to severe bleeding (N = 1419)*

	Secondary procedure	No secondary procedure
Number of patients	111 (7.8%)	1308 (92.2%)
Age (years) (mean ± SD)	33.3 ± 8.2	35.2 ± 8.9
Age range	13–60	13–85
Nulliparous	16 (14.4%)	215 (16.4%)
Multiparous	95 (85.6%)	1093 (83.6%)

SD: standard deviation; Differences in age: $t = 0.03$; $P>0.05$; Differences in parity: $\chi^2 = 0.18$; $P>0.05$

Table 2. *Secondary procedures due to post–LLETZ bleeding in patients with and without genital pathogens (N = 1419)*

	Genital pathogens present (N = 714)	Genital pathogens absent (N = 705)
No secondary procedure	651 (91.2%)	657 (93.2%)
Secondary procedure	63 (8.8%)	48 (6.8%)
Vaginal pack	46 (6.4%)	32 (4.5%)
Sutures	24 (3.4%)	15 (2.1%)
Hysterectomy	0	1 (0.1%)

Difference in the prevalence of secondary procedures between patients with and without genital pathogens: $\chi 2 = 1.72$; $P>0.05$).

DISCUSSION

The present study showed that secondary procedures due to severe bleeding were required in fewer than 8% of cases.

In accordance with our findings, studies have demonstrated a high prevalence of adverse effects after LLETZ if these were sought by means of a questionnaire and a much lower prevalence if adverse effects were identified by reviewing charts. The Trial of Management of Borderline and Other Low Grade Abnormal Smears (TOMBOLA) group studied 751 women who completed a questionnaire on after–effects 6 weeks after LLETZ, and found that 87% of study participants reported bleeding (8). In a retrospective review of 557 charts, Dunn et al. described bleeding after LLETZ in 4.8% of patients and the need for secondary procedures due to bleeding in 1.4% of subjects (7). Likewise, Ljubojević et al. reported the prevalence of moderate postoperative haemorrhage from the excision site to be 5.5% (16). Similarly, Girardi et al. found a prevalence of postoperative bleeding in 5.3% of patients (17) and Hallam et al. found a prevalence of severe haemorrhage of 3.8% (18).

We found that patients who needed secondary procedures and those who did not were of a similar age and parity. In our previous study on the role of *Chlamydia trachomatis* infection in bleeding after LLETZ, we found that patients with bleeding were significantly younger than those without bleeding and more frequently nulliparous (although this difference was not significant) (15). Considering the results from the present study, we believe that the previously reported differences were probably coincidental.

The present study showed that half of all women who were treated with LLETZ were harbouring genital pathogens. It is well known that cervical pathogens are common among women and do not always cause symptoms (19, 20).

We discovered that a secondary treatment procedure because of haemorrhage was not carried out significantly more often in the group of patients with infection of the genital tract. In a prospective study of 48 women treated with LLETZ, Sarkar et al. found that 56% of patients were harbouring genital pathogens. They did not observe a significant difference between the mean duration of post–LLETZ bleeding in patients with and without genital pathogens. However, among women who graded their bleeding as 'moderate' or 'severe', post–procedure haemorrhage lasted significantly longer in those with infection of the genital tract (14).

Chan et al. carried out a prospective, randomized controlled trial investigating the influence of topical tetracycline and amphotericin B after LLETZ on the prevalence of complications. Among the 321 patients in their study, they identified a subgroup of women with positive endocervical or high vaginal swabs who had significantly less bleeding in the second week when treated with topical antimicrobial agents. However, no significant benefit of the treatment was demonstrated for the general population (21).

In addition, Gornall et al. carried out a randomised trial involving 100 patients who received local treatment with sultrin pessaries for 5 days after LLETZ or who did not have treatment. They described no significant difference in the severity of vaginal bleeding or other symptoms between the two groups, and did not recommend prophylactic topical treatment (22).

In conclusion, the results of the present study show that infection of the uterine cervix does not have a role in severe secondary bleeding necessitating revision procedures after LLETZ.

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