



CLINICAL ARTICLE

Large loop excision and cold coagulation for management of cervical intraepithelial neoplasia

M. Allam, A. Paterson, A. Thomson, B. Ray, C. Rajagopalan, G. Sarkar*

Department of Obstetrics and Gynaecology, Royal Alexandra Hospital, Corsebar Road,
Paisley, PA2 9PN, UK

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Abstract

Objectives: To evaluate the efficacy of large loop excision of the transformation zone (LLETZ) combined with a single application of the cone probe of a Semm Cold Coagulator as a new treatment for women with cervical intraepithelial neoplasia (CIN). **Methods:** Retrospective case-record review of 666 women treated with large loop excision and cold coagulation (LLECC) from 1992 to 2000. **Results:** Of the women who had high-grade CIN at their initial consultation, 4.2% had abnormal cytologic results 6 months after treatment and 0.6% had abnormal cytologic results at 12 months. Of the women who had low-grade CIN at initial presentation, 3.8% had abnormal cytologic results 6 months after treatment and none (0%) at 12 months. Furthermore, there were no reported cases of cervical cancer in this cohort of women during the follow-up period. Short-term bleeding complications (within 24 h of the procedure) occurred in 1% of the women assessed. **Conclusions:** Large loop excision combined with cold coagulation is a new and effective treatment for CIN. Randomized controlled trials are required to confirm these findings and determine the long-term safety of the technique.

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1. Introduction

Cervical intraepithelial neoplasia (CIN) has been treated in many different ways that include various ablative and excisional procedures [1]. Treating women with CIN reduces the risk of invasive cervical cancer by 95% [2,3], and meta-analyses

* Corresponding author. Tel.: +44 141 887 9111; fax: +44 141 580 4364.

E-mail address: Gour.Sarkar@rah.scot.nhs.uk (G. Sarkar).

have concluded that there is no obviously superior surgical or hemostatic technique for the management of CIN [4,5]. Large loop excision of the transformation zone (LLETZ) is the preferred method of treating CIN in both the United Kingdom and the United States. It is associated with low morbidity [6–8], provides tissue for histopathologic assessment, and is as effective in the short term as ablative treatments, which it has largely replaced [9–14].

The reported rates of therapeutic effectiveness for LLETZ and other treatment procedures range from 60% to 95% [15]. Most treatment failures of CIN, regardless of the technique employed, will become apparent during the first year of follow-up [16,17]. Hammond [17] concluded that posttreatment dyskaryosis may cause considerable management dilemmas if colposcopic assessment becomes less reliable. Furthermore, patient anxiety is understandably increased by the news of a cytological abnormality [18,19]. One of the most commonly reported short-term complications of LLETZ is hemorrhage, which occurs in up to 2.6% of women in the first 24 h after treatment [20,21].

Since 1992, women with CIN attending our unit have been treated using a modified version of LLETZ combined with a single application of the cone probe of a Semm Cold Coagulator (Wisap, Sauerlach, Germany). The probe is heated to 120 °C, then applied for 20 s to the crater produced by LLETZ. This method, large loop excision and cold coagulation (LLECC), was introduced to our colposcopy unit by one of the authors (GS) to minimise hemorrhagic complications. Regular audits of the colposcopy clinic performance have suggested that LLECC might be beneficial both as a hemostatic technique and for reducing the proportion of abnormal smears at follow-up. With conventional LLETZ, ball diathermy is frequently used for hemostasis rather than the Semm Cold Coagulator.

The purpose of this study was to determine the efficacy of LLECC at 12 months as a new treatment for patients with CIN and to evaluate the short-term hemorrhagic complications of this technique.

2. Materials and methods

A retrospective review of the case records of 666 women with CIN was carried out. All women were diagnosed by histologic studies in the colposcopy clinic of a district general teaching hospital between 1992 and 2000. Those treated with LLECC were identified and results from cytologic and

histologic studies were analyzed. Microsoft Excel was used for data analysis.

Visualisation of the complete squamocolumnar junction and exclusion of any suspicion of invasion were the criteria for LLECC treatment. Verbal consent was obtained prior to treatment. The LLETZ component was performed by colposcopists of various experience using a standard technique [22]. Following colposcopic assessment, the stroma of the cervix outside the transformation zone was infiltrated with 4 mL of a local anesthetic (prilocaine hydrochloride, 30 mg/mL and felypressin, 0.03 U/mL (Citanest with Octapressin; Dentsply, Surrey, UK). There were no documented adverse reactions to this local anesthetic preparation. A Valleylab Force 2 electrosurgical unit (Valleylab, Colo, USA) was used, together with a wire loop of appropriate size to excise the transformation zone, with the generator set on both cutting and coagulation. Following LLETZ, cold coagulation was performed by applying the cone probe of the Semm Cold Coagulator to the crater. The probe was heated to 120 °C and applied to the cervix for 20 s.

All grades of CIN were treated in the same way. Initially, LLECC treatment was performed during the second visit, after punch biopsy results were obtained. As experience developed, a “see and treat” policy was implemented. At the 6- and 12-month follow-up visits, all women were seen at the colposcopy clinic where a colposcopic examination and a Pap smear were performed. If these two assessments gave normal results, the women were referred to their general practitioner with a recommendation of five annual smears before a return to routine screening. Women with positive cytologic results were reviewed colposcopically, and management strategies were chosen depending on colposcopy findings. These were not analyzed in this study. Treatment failure was classified as persistent disease.

3. Results

The records of 666 women in whom LLECC was performed between 1992 and 2000 were reviewed. The mean $\pm$ S.D. age was 33 $\pm$ 8.2 years.

At initial presentation, 576 (86.4%) of the 666 women had high-grade CIN (CIN II and CIN III), and 90 (13.5%) had low-grade CIN (CIN I). The 6-month follow-up visit was not attended by 63 women (9.5%), leaving 603 women (90.5%) for analysis. At 12 months, data were available for 541 of 578 (93.6%) women, after a further 37 of 578 women (6.4%) did not attend the follow-up visit (women

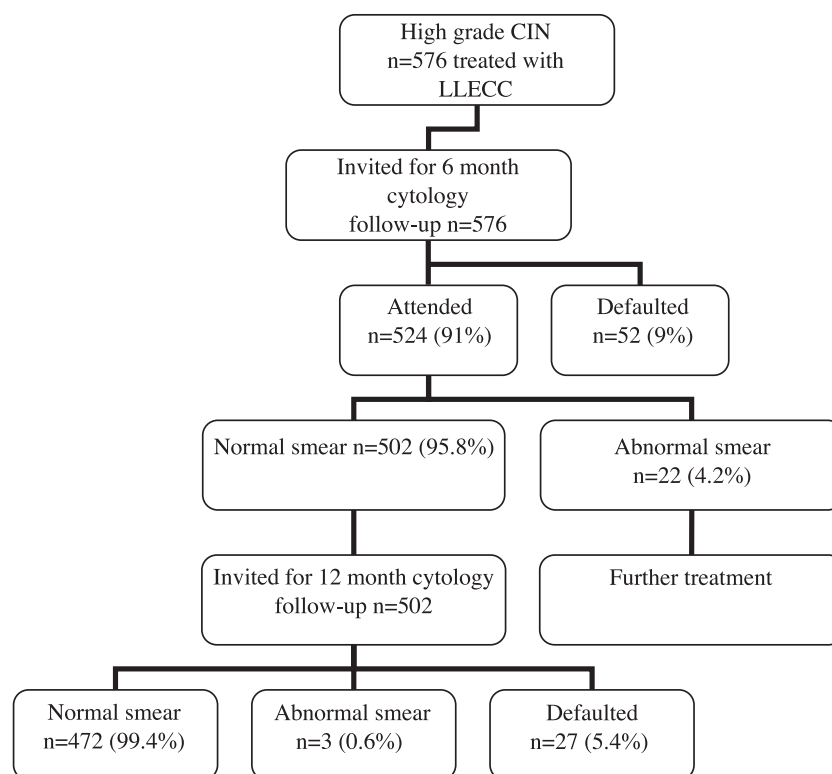


Figure 1 Study profile of women with high grade CIN at initial presentation.

with nonavailable data were excluded from further study at each stage) (Figs. 1 and 2).

Of the 524 women who had high-grade CIN at initial presentation, 22 (4.2%) had an abnormal smear 6 months after treatment. These women, in whom LLECC management had failed, underwent

further treatment and were excluded from the 12-month follow-up assessment. Of the remaining 502 women who had high-grade CIN at initial presentation, 3 (0.6%) had abnormal cytologic results at 12 months (Table 1). Of the 79 (3.8%) women who had low-grade CIN, 3 of had an abnormal smear at 6

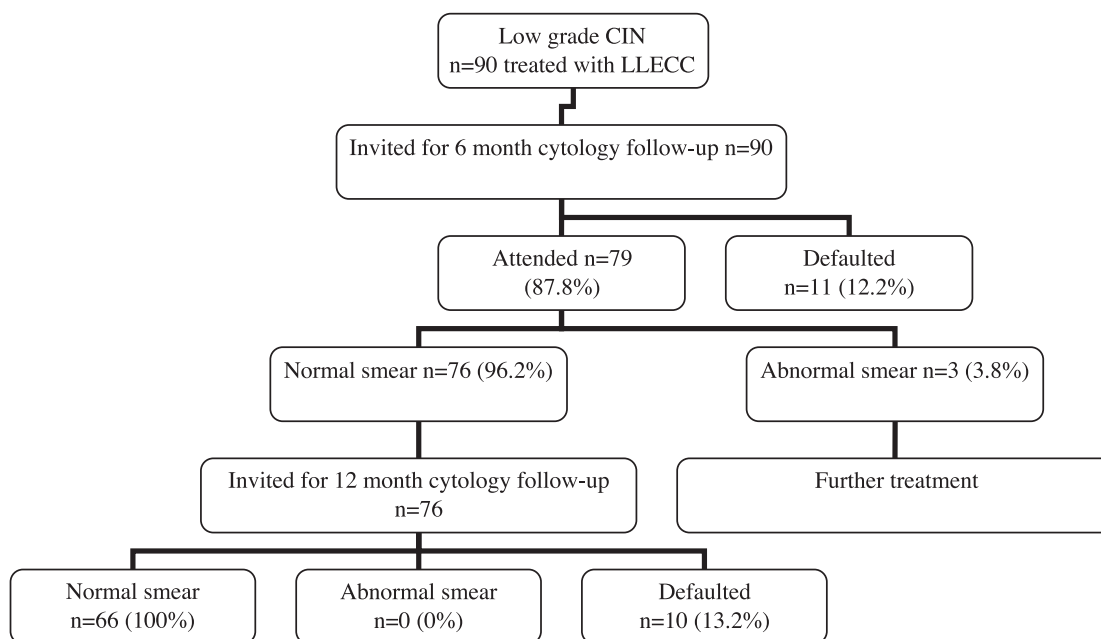


Figure 2 Study profile of the women with low-grade CIN at initial presentation.

Table 1 Results of follow-up cervical cytology in the 666 women treated with LLECC in the study

Initial histologic finding	Excision of CIN complete	Excision of CIN incomplete	Cytology result at 6 months		Cytology result at 12 months	
CIN I (n=90)	69	5	Normal	76	Normal	66
			Mild dyskaryosis	2	Mild dyskaryosis	0
			Moderate dyskaryosis	1	Moderate dyskaryosis	0
			Severe dyskaryosis	0	Severe dyskaryosis	0
CIN II and III (n=576)	417	86	Normal	502	Normal	472
			Mild dyskaryosis	13	Mild dyskaryosis	0
			Moderate dyskaryosis	1	Moderate dyskaryosis	1
			Severe dyskaryosis	8	Severe dyskaryosis	2

When abnormal cervical cytology was obtained at follow-up, the women received further treatment and were excluded from further study. Women who did not attend at each stage of follow up were also excluded. The numbers of women who received further treatment and who defaulted from follow-up are shown in the figures.

months, and 0 of the 66 who attended the second follow-up visit had abnormal cytologic results at 12 months (Table 1). Furthermore, there were no reported cases of cervical cancer in this cohort during the follow-up period.

In 89 (4%) of the 666 cases, the histologic report did not specify whether the CIN excision by the LLETZ component of our treatment was complete or incomplete. The pathologist noted that excision of CIN was complete in 486 (84%) of the remaining 577 women (86.6%) and incomplete in 91 (16%). In women with high-grade CIN, excision of the lesion was complete in 417 of 576 women (72.4%) and incomplete in 86 (14.9%). The results of cervical cytologic evaluation were abnormal at 6 months in 16 (2.7%) of the 603 women whose initial CIN lesion was excised incompletely, and abnormal at 12 months in 2 (0.4%) of 541 (Table 2). The mean $\pm$ S.D. depth of the LLETZ biopsies was 6 ± 3 mm.

Data on short-term bleeding complications (within 24 h of the procedure) were retrieved from 275 case records (41.3%). It occurred in 3 (1%) of the 275 cases analyzed. One woman required sutures to achieve hemostasis. None of the three

women required blood transfusion or in-patient hospital admission.

4. Discussion

While LLETZ is the accepted treatment for the management of CIN in the United Kingdom and the United States [6–8], recent Cochrane systematic reviews concluded that there is no superiorly effective treatment or hemostatic technique for the management of CIN [4 5]. The recommended standard percentage of persistence of abnormal smear 6 months after treatment, 10%, set by the National Health Service Cancer Screening Programmes, is yet to be met by many units in the United Kingdom [23]. A persistence rate of abnormal cytologic results between 15% and 39% is not infrequently quoted [1,3,15]. Failure rates between 5% and 22% 1 year after treatment with the Semm Cold Coagulator are cited, and the higher percentages are associated with high-grade CIN [24]. In the present study, the decision was made to assess follow-up cervical cytologic results 6 and 12 months after treatment because Bigrigg and Flannelly and others [9,14,16,17] have shown that most treatment failures will become apparent during this time.

It is now well established that women with clear margins have a low risk of recurrence, approximately 5% [25]. The management of women in whom margins of resection are involved, on the other hand, remains unresolved because these women have a higher and variable risk of recurrence. The reported rates of treatment failure following incomplete excision of CIN vary between 3.6% and 44% [25]. In our cohort, there was a relatively high rate of incomplete excision (16%) associated with a shallow depth of LLETZ (mean depth, 6 mm)—which may be related to the number

Table 2 Smear results at 6 and 12 months according to the completeness/uncompleteness of excision

	Normal smear, 6 months	Abnormal smear, 6 months	Normal smear, 12 months	Abnormal smear, 12 months
Attendance for follow up	n=578/603	n=25/603	n=538/541	n=3/541
Complete	498/603 (82.5%)	9/603 (1.5%)	453/541 (83.7%)	1/541 (0.002%)
Incomplete	81/603 (13.4%)	16/603 (2.7%)	85/541 (15.7%)	2/541 (0.4%)

Total number of women attending at 6 months follow-up=603. Total number of women attending at 12 months follow-up=541.

of colposcopists and their various levels of experience. Despite these findings, the results presented in this study (cervical cytologic results at 6 and 12 months) using LLECC were at least as good as the results from published series using LLETZ alone [14,15]. Using LLECC, the persistence rate of abnormal smears after 1 year was 0% for low-grade CIN and 0.6% for high-grade CIN. Furthermore, more than 70% of the women treated with LLECC had high-grade CIN. In this study, the rate of abnormal cervical cytologic findings in women who had incomplete excision of their initial lesion was 4.2% at 6 months and 0.4% at 12 months. These results suggest that treatment of CIN using LLECC may be better than LLETZ alone, although this needs to be investigated further in a large prospective randomized controlled trial.

The rate of posttreatment bleeding with LLECC was 1%, compared with the rates of 2% and 2.6% reported by others for LLETZ [20,21]. This low incidence of short-term bleeding complications with LLECC is encouraging, but needs to be addressed further in prospective trials. The potential long-term cervical complications of LLECC, such as cervical stenosis and cervical incompetence, were not assessed in this study. Wright et al. [20] reported a rate of cervical stenosis of less than 1% following treatment with LLETZ, and Luesley et al. [10] reported an incidence of cervical stenosis (defined as the inability to pass a Hegar 3 probe into the endocervix) of 1.3% (all women with cervical stenosis had an excision deeper than 14 mm). Furthermore, Duncan reported cases of cervical stenosis requiring dilatation because of interference with menstrual flow in up to 1% of patients as a late complication after cold coagulation [24]. It would be unlikely for LLECC to have a high incidence of these complications since the maximum depth of cervical destruction using cold coagulation (30 s at 120 °C) is only 4 mm [26].

The authors have observed that the cold coagulator probe fits easily and uniformly into the LLETZ crater, even with difficult positions of the cervix, and suggest that this phenomenon may have contributed to the low rate of both hemorrhagic complications and persistence of abnormal smears—for the latter, by avoiding the creation of skip lesions. It is proposed that the use of LLECC may be beneficial for the management of CIN in countries where less experienced staff provide colposcopy services; in all units not achieving the required RCOG/BSCCP standards with “conventional” LLETZ; and when patients are less likely to attend their follow-up visits. One disadvantage of LLECC is that the cone

probes of the cold coagulator provide additional purchasing and maintenance costs. These additional costs may be justified if LLECC is shown in prospective trials to be a more effective treatment than LLETZ, thereby resulting in fewer treatment failures.

5. Conclusions

Large loop excision of the transformation zone combined with cold coagulation is a new and effective approach for the treatment of CIN. Its clinical, psychological, and financial implications may be significant but they still need to be assessed. Prospective, randomized, controlled trials are required to confirm these results, and to determine the optimum duration of cold coagulation and the possible long-term complications of the technique.

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