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Efficacy of cervical intrarepithelial neoplasia (CIN) treatment by cold coagulation

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SUMMARY

Our objective was to evaluate the efficacy of cold coagulation in the treatment of cervical intraepithelial neoplasia. The study design consisted of a retrospective review of case records of all women treated with cold coagulation from the colposcopy clinics inception in 1980 to 1994. A total of 725 women received treatment with cold coagulation. All grades of CIN were treated. 632 (87.1%) had long term negative follow up. 93(12.6%) of patients had abnormal cytological follow up, but only 45(6.2%) required re-treatment. Within the first year after treatment 52(7.1%) patients presented with persistent cytological abnormalities, 32(4.4%) required repeated treatment for persistent dyskaryosis. 41(5.6%) of patients had recurrent cytological abnormalities, 13(1.8%) required repeated treatment. Recurrence developed between two and 12 years from initial treatment. One case of cervical carcinoma following treatment with cold coagulation was recorded. Our data suggest that cold coagulation appears to be safe, efficient treatment for cervical intraepithelial neoplasia.

INTRODUCTION

Cold coagulation is one of many ablative methods designed to destroy an abnormal transformation zone. It has been successfully used to treat non-invasive cervical conditions since 1966. This treatment method was introduced to clinical practice for the first time by Kurt Semm;[1] it became a popular method for the treatment of CIN. In the1980s it was the second most popular treatment modality, for CIN in the UK. It has, however, lost some of its popularity due to the introduction of the Large Loop Excision of the Transformation Zone (LLETZ) performed under local anaesthesia. The latter, being an excisional rnethod, secured the whole transformation zone for histopathological examination.

Cold coagulation is a suitable therapy for the out-patient clinic. It is a relatively painless procedure requiring minimal or no analgesia. It is also user and patient friendly having a short treatment time, and virtually no immediate complications. All grades of CIN may be treated with cold coagulation.

The purpose of this study is to evaluate the efficacy of cold coagulation in the relatively static population of women treated in Belfast City Hospital colposcopy clinic.

PATIENTS AND METHODS

We reviewed the notes of patients who had attended the BCH colposcopy clinic between its establishment in 1980 and 1994. Patients treated with cold coagulation were identified and their medical records and cytology results were analysed.

The cytological results were obtained from the BCH Cytology Laboratory computer and the Northern Ireland Cervical Screening Programme database. Information regarding women attending other hospitals after initial treatment with cold

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coagulation at BCH was traced. Microsoft Excel was used for data analysis.

Standard management at the clinic consisted of colposcopic examination with confirmatory biopsy. Visualisation of the complete squamo-columnar junction and exclusion of any suspicions of invasion were the criteria required for cold coagulation treatment. Verbal consent was routinely obtained prior to treatment.

When suitable, patients were offered treatment with cold coagulation under local anaesthesia. Treatment was preceded by punch biopsy. All grades of CIN were treated in the same way by application of the Semm coagulator (WISAP, Germany) to the cervix. The probe heated to 120°C was applied to each part of the cervix for 30-40 sec. ensuring that the whole transformation zone was destroyed beyond the limit of aceto-white epithelium. All patients were advised to apply Sultrin cream (Janssen-Cilag) vaginally, nightly for one week and to avoid intercourse and use of tampons for three weeks.

Initially treatment was performed during the second visit, but as experience developed a "see, biopsy and treat" policy was employed, with only less experienced or trainee colposcopists awaiting biopsy results before treatment.

The pattern of follow up changed over the years of study, but all patients were followed up by at least cytological assessment. This was initially performed at the 3-4 months follow-up visit. Since 1990 follow-up has been by a standard pattern of review and smear by the hospital at six months post treatment. If this smear is normal, the patient attends her GP for a further smear at six months post treatment. Thereafter yearly smears are advised.

Patients with positive cytological results were reviewed colposcopically and various regimens of management were instituted depending on colposcopy findings and individual practice.

Failure of treatment was classified into two groups for the purpose of this study; persistent disease was recognised when abnormalities were identified between 6-12 months following initial treatment, recurrent disease if abnormalities appeared after 12 months.

Further management of patients with abnormal follow up cytology included repeat cold coagulation, Large Loop Excision of the Transformation Zone, cold knife biopsy and hysterectomy.

RESULTS

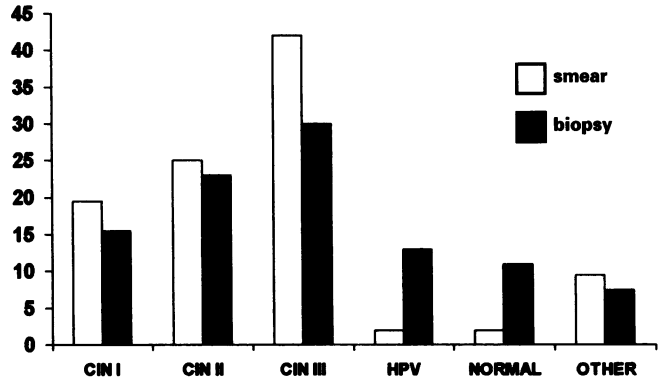
Out of 1329 patients attending the colposcopy clinic 725 (54.5%) patients received treatment with cold coagulation.

The mean age of patients at presentation was 28 years and ranged from 17 to 52 years. 35% of patients were nulliparous, 18% had one child, 19% had two children, and 12% had three or more children.

Distribution of referral smear findings and initial biopsy results are shown in Figure. 632(87.2%) patients had dyskaryotic abnormalities eradicated by initial cold coagulation treatment and their long term cytological follow up was negative. 93(12.8%) patients developed abnormal smear at some stage after treatment. 52 patients(7.1%) presented with persistent cytological abnormalities within the first year of treatment and 41(5.6%) with recurrent abnormal smears.

FIGURE

Distribution of referral smears and biopsies results, 95% of treated patients had biopsy taken prior to treatment.



Of the 52 patients with persistent abnormal cytological results 27(52%) presented with CIN III on referral smear, 12(23%) with CIN II and 6(12%) with CIN I, 3(6%) patients had unclassified CIN.

Of these 52 patients showing persistent cytological abnormalities 31(4.3% of all treated with cold coagulation) had further treatment, 20 on the basis of positive biopsy and 10 on colposcopic appearance (Table I).

21 patients were given no further treatment and were considered to have transient cytological

TABLE I

Management of patients with persistent cytological abnormalities

Smear results	*No*	*Biopsy results*	*No*	*Treatment*	*Recent smear No*		*No*
HPV	13	No biopsy	8	No treatment	8	N/a-TAH (hist.neg)	1
						Negative	7
		HPV	5	Cold coagulation	5	Negative	5
CIN	39	Dysplasia	16	Various treatment **(table 3)**			
		No biopsy	4	Cold coagulation	4	Negative	3
						BNA	1
		No biopsy	6	LLETZ (hist.neg)	6	Negative	5
						N/a-TAH (hist.neg)	1
		Biopsy negative	2	No treatment	2	Negative	2
		Biopsy positive	1	No treatment	1	Negative	1
		No biopsy	10	No treatment	10	Negative	5
						N/a-TAH (hist.neg)	1
						Defaulted	3
						Recurrence	1

HPV-human papillomavirus infection, CIN-cervical intraepithelial neoplasia, n/a-not applicable, TAH-total abdominal hysterectomy, hist.neg – histopathology results negative, LLETZ – large loop excision of the transformation zone.

abnormalities. 17 patients of this untreated group had negative follow up. Three of these patients have been lost to long term follow up, one patient had negative screening for five years and presented at sixth year with recurrent low grade disease. The treatment modalities of those who received subsequent treatment are summarised in Table II.

Hysterectomy was usually offered as a treatment option when other gynaecological problems were present. Of 9 hysterectomies performed seven uterine specimens showed no evidence of residual CIN.

Overall, 40% of patients with persistent cytological abnormalities at 4-6 months following treatment required no further treatment as abnormalities reverted to normal, suggesting that the rate of residual disease was less that 7, 1% already stated.

Recurrent disease was defined as abnormalities developing more than a year after treatment. 41(5.6%) patients treated with cold coagulation developed recurrent abnormal smears. These patients presented between two and 13 years from initial treatment.

26(3.5%) of them developed abnormal smears within first 5 years from treatment, a further 12 patients(1.6%) between year 6 and 10, three patients(0.4%) had recurrence more then 10 years following treatment (Table III).

Of those with recurrent abnormalities 18(44%) presented with CIN III on referral smear, 8 patients (19%) with CIN II, 6(15%) with CIN I, 5(12%) with unclassified CIN, 3 (7%) borderlines and 1 (2.4%) with normal cytology.

Out of 41 recurrent cytological abnormalities the majority (26 cases) were low grade abnormalities: 8 borderline nuclear abnormalities, 8 viral infections and 10 CIN I. Overall, recurrent abnormalities included 25 patients with dyskaryotic smears, 8 with recent borderline smears and 8 with transient viral changes.

TABLE II

Management of 16 patients with persistent cytological abnormalities confirmed by biopsy.

Referral smear	*No*	*Second treatment*	*No*	*Recent smear*	*No*
CIN 1	1	TAH	1	N/a	1
CIN 11	2	TAH	1	N/a	
		Cone biopsy	1	Lost from follow up	1
CIN Ill	12	Cone biopsy	12	Negative	5
				N/a-TAH	4
				-rad.hyst	1
				-died	1
				Lost from follow up	1
Not recorded	1	Cone biopsy	1	negative	1

N/a- not applicable, TAH-total abdominal hysterectomy, cone biopsy-any excisional surgery, rad.hyst.-radical hysterectomy

TABLE III

Management of patients with recurrent cytological abnormalities

Recurrent smear	*No*	*Management*	*No*	*Recent smear*	*No*
HPV	8	No treatment	8	negative	8
BNA	8	Awaiting further assessment	8		
CIN I	10	Cone biopsy	3	Negative	3
		Cold coagulation	1	Negative	1
		No treatment	3	Negative	2
				Lost	1
		Awaiting assessment	3		
CIN II	6	Cone biopsy	2	Negative	2
		Cold coagulation	1	Lost	1
		Cautery	1	Negative	1
		No treatment	2	Negative	2
CIN Ill	6	Cone biopsy	4	N/a-TAH	3
				Lost	1
No treatment	2	Negative	2		
CIN unclassified	3	Cone biopsy	1	Negative	1
		No treatment	2	Negative	2

N/a -not applicable, TAH – total abdominal hysterectomy, cone biopsy – any excisional surgery

6 patients had recurrent severe dyskaryotic smears. All of them presented with initial, referral CIN III and recurred within 5 years of initial treatment. 13(1.8%) patients received treatment for recurrent dyskaryosis, 10 of them were treated with excisional surgery, 3 with ablative methods. 28 patients did not receive treatment, 11 of them had low grade, transient abnormalities, 11 had recent positive cytology (8 borderline and 3 CIN I) and have been awaiting further assessment, and 6 had transient dyskaryotic smears which reverted to normal and remain so.

8 patients (1.1%) had complications recorded in their notes: 2 vaso-vagal faints, 5 cervical bleeding related to the biopsy site, and 1 secondary haemorrhage due to infection.

The only case of invasive disease following treatment with cold coagulation occurred in 1987. This patient was referred to the clinic in 1984, at the age of 23 following conisation of cervix for CIN III in another hospital. Colposcopy showed widespread dysplastic changes; smear CIN II and biopsy CIN II. She was treated with cold coagulation under general anaesthesia. Follow up smears were persistently abnormal. This patient underwent five further treatments to the cervix with different modalities for persistent dyskaryotic abnormalities. The last excision revealed invasive squamous carcinoma of cervix. She was treated successfully with radical hysterectomy and has been in regular follow up.

Out of 725 patients treated with cold coagulation 699(96, 4%) had at least a first follow-up smear and 587 (80.9%) have up to date negative follow-up smear. 106(14.6%) are lost from follow up: 42 emigrated, 64 can't be traced or refuse to have a smear, 2 died of other causes, 19(2.6%) patients had hysterectomy performed. 11(1.5%) patients have recent positive smears: 8 borderline and 3 mild dyskaryosis. Default rate at first follow up was 12%(87 patients). These patients failed to have first follow-up smear after treatment. However, 56 of them have an up to date smear, 19 emigrated, 2 had TAH and only 7(0.9%) of all treated patients) of them are truly lost to follow up.

Overall of 725 patients treated with cold coagulation 44 patients (6%) received repeated treatment for persistent or recurrent disease. 10 (1.3%) patients with recent abnormal smear have been awaiting further assessment. The success rate of treatment with cold coagulation in long term follow up at our colposcopy clinic was 92.7%.

DISCUSSION

A computerised call/re-call system for cervical screening was established in Northern Ireland in 1989. The results of all smears are held on a single data bank. There are 460,000 women aged 20 to 65 eligible for cervical screening in Northern Ireland. The recommended normal recall interval is 5 years and women are called to attend for cervical smear from the age 20. The response rate is still low at 67%.[2]

Every year 80 new cases of cervical carcinoma (including microinvasion) are detected in Northern Ireland, giving the prevalence of 9.6 per 100,000 women.[2] Of these cases 50% of women were unscreened, 7% screened more than 5 years before the occurrence, 26% had negative smear 5 years before and 16% had previous abnormal smear. The latter group consists of patients treated, who defaulted or who refused treatment. There was no incidence of invasive cervical carcinoma among teenagers in Northern Ireland.

In our setting, cold coagulation has been shown to be a safe and efficient treatment with a very low morbidity rate. This is in keeping with earlier work by Duncan[3, 4, 5] Cold coagulation was shown to be well accepted by both patients and colposcopists. However, it requires a competent colposcopist and compliance with strict selection of patients suitable for treatment with cold coagulation as established by Gordon and Duncan. Obviously a suspicion of invasion or unsatisfactory colposcopic assessment excludes any ablative method of treatment. Gordon and Duncan[3] claimed 95% primary success rate for CIN III and success rate of 96.5% with single treatment and 99% following one or more treatments with cold coagulation for patients with CIN I and CIN.[4] Our results are comparable with these studies. Despite these satisfactory results it has still been questioned whether or not cold coagulation can efficiently treat CIN lesions. The long term follow-up with persistent negative cytology illustrated by this study and those of Duncan and co-workers confirm the effectiveness of this treatment. Results of our study indicated a very low rate(7.1%) of persistent disease, much lower than reported by Semple.[6] He reported 14.8% rate of persistent abnormalities following CIN treatment with all modalities used by 19

colposcopy clinics in North West. The recurrence rate following treatment with cold coagulation is very low, 5.6% in our study, with mainly low grade abnormalities being found at follow-up. Not surprisingly we found the highest level of treatment failure among CIN III lesions which accounted for 42% of referred cases. It is our opinion that previous treatment to the cervix, as a factor changing its anatomy is a contraindication for cold coagulation treatment. The only case of invasive cancer of cervix following treatment with cold coagulation occurred in a woman who had previously had treatment to her cervix, which distorted the anatomy preventing the full lesion from being amenable to cold coagulation, although it should be noted that several attempts had been made to excise persistent abnormalities before she developed invasive disease. During the study period there were 10 cases of carcinoma of cervix diagnosed on histopathology as a result of excisional biopsies, which had not been colposcopically detected. All of these patients had unsatisfactory colposcopy, therefore had been considered unsuitable for treatment with cold coagulation and were treated by excislonal techniques.

We have not encountered unexpected histopathology results of microinvasive or invasive carcinoma from biopsies taken prior to the cold coagulation treatment.

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REFERENCES

1. Duncan I D. Cold coagulation. *Baillieres Clin Obstet Gynaecol* 1995; **9(1)**: 145-55.
2. Quality Assurance Northern Ireland Cervical Screening Programme. In press.
3. Gordon H K, Duncan I D. Effective destruction of cervical intraepithelial neoplasia (CIN) 3 at 100 degress C using the Semm cold coagulator: 14 years experience. *Br J Obstet Gynaecol* 1991; **98(1)**: 14-20.
4. Loobuyck H A, Duncan I D. Destruction of CIN 1 and 2 with the Semm cold coagulator: 13 years experience with a see-and-treat policy. *Br J Obstet Gynaecol* 1993; **100(5)**: 465-68.
5. Duncan I D, editor. Guidelines for clinical practice and programme management. Sheffield: NHS Cervical Screening Programme, 1997.
6. Semple D, Saha A, Maresh M. Colposcopy and treatment of cervical intra-epithelial neoplasia: are national standards achievable. *Br J Obstet Gynaecol* 1999; **106(4)**: 351-55.