

An evaluation of treatment modalities in cervical intra-epithelial neoplasia

J. ATAD, B. BLOCH

Summary

The scheme of management of cervical intra-epithelial neoplasia presently utilized in the colposcopy service at Groote Schuur Hospital, Cape Town, is outlined, and the results of the treatment of 721 patients with the various modalities currently available are analysed. It is concluded that a radical

approach (total hysterectomy was performed in 42.4% of the patients) is justified by the results obtained; the place of conservative methods of treatment, including cone biopsy, is discussed.

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Department of Gynecology, Mount Carmel Hospital, Haifa, Israel

J. ATAD, M.D.

Department of Obstetrics and Gynaecology, University of Cape Town and Groote Schuur Hospital, Cape Town

B. BLOCH, M.MED. (O. & G.), F.R.C.O.G.

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Although the forms of treatment available for the treatment of cervical intra-epithelial neoplasia (CIN) have been evaluated in various clinical settings, considerable differences of opinion still exist, mainly because of the ethnic, educational and cultural diversity of population groups encountered in various parts of the world. In particular, follow-up attendances during and after therapy, the mobility of certain racial groups in this country and the facilities for tracing patients who habitually default are factors which, of necessity, must be taken into account when determining the most effective form of treatment for an individual patient.

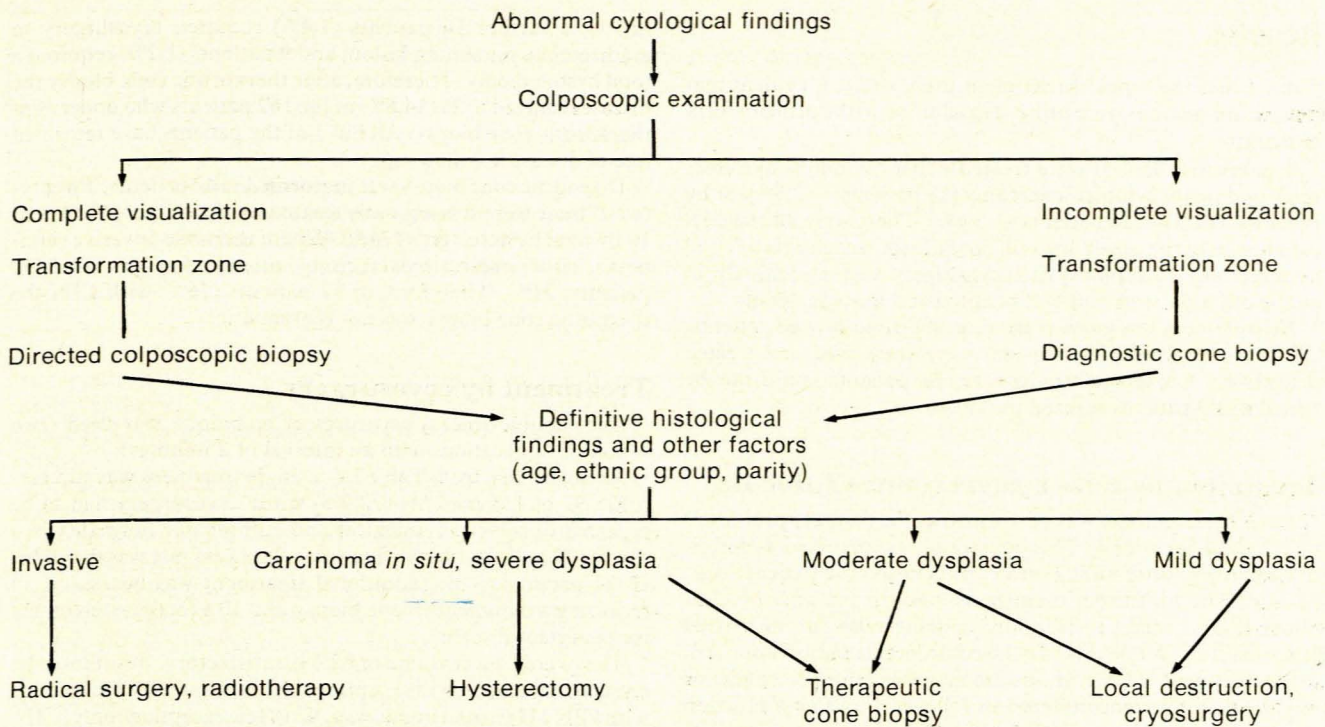


Fig. 1. Scheme of management.

As part of a prospective study into the training of registrars in colposcopy the modalities of treatment together with their individual problem areas and success rates were evaluated; these data are presented.

Patients and methods

The records of 750 consecutive patients seen at the Grootte Schuur Hospital Colposcopy Clinic, Cape Town, were analysed in order to assess: (i) the types of treatment utilized and their respective incidences of usage; (ii) the success rates of the various forms of treatment; and (iii) whether the scheme of management now in use (Fig. 1) is cost-effective and provides optimum

patient care. Data on the patients have been provided in a previous article.¹ Information on 29 of these patients was incomplete, leaving 721 patients available for study.

The cytological abnormality at the time of referral for colposcopy has been detailed;¹ of the 721 patients no fewer than 551 (76,4%) had serious intra-epithelial lesions, while 72 (10%) had micro-invasive or invasive cancer. The decisions regarding treatment were made after histological confirmation of the colposcopic and cytological reports. The correlation between these diagnostic methods has been reported elsewhere.¹ The follow-up period was a minimum of 8 months, but in most instances was from 12 to 18 months, during which period the vast majority of recurrences would have been expected to become apparent.²

TABLE I. TREATMENT MODALITIES

	No.	%
Total hysterectomy, vaginal and abdominal	277	38,4
Radical hysterectomy	18	2,5
Radiation therapy	26	3,6
Therapeutic cone biopsy	138	19,1
Therapeutic cone biopsy and cryosurgery	10	1,4
Therapeutic cone biopsy, total hysterectomy	9	1,2
Repeat therapeutic cone biopsy	5	0,7
Diagnostic cone biopsy*	42	5,8
Followed by cryosurgery	22	3,1
Followed by total hysterectomy	10	1,4
Followed by radical hysterectomy and radiation	10	1,4
Cryosurgery (single treatment)	97	13,4
Cryosurgery and therapeutic cone biopsy	14	1,9
Cryosurgery and repeat cryosurgery	12	1,7
Cryosurgery and total hysterectomy	10	1,4
No treatment†	63	8,7
Total	721	

*Diagnostic procedure only.

†33 patients were pregnant, 21 defaulted, and 9 refused treatment.

Results

Table I lists the types of treatment used, and it is evident that many combinations were utilized in addition to the primary form of therapy.

The invasive lesions were treated either by radical hysterectomy and pelvic lymphadenectomy (18 patients — 2,5%), or by radiation therapy (26 patients — 3,6%). These were all stage IB carcinomas of the cervix and will not be discussed in detail. Total hysterectomy, cone biopsy and cryosurgery were used initially in all the other patients and will be discussed in some detail.

No treatment was given at the time of diagnosis in 63 patients. Of these, 33 were pregnant and were reassessed and treated definitively 6 weeks after delivery, 21 patients could not be traced and 9 patients refused treatment.

Treatment by total hysterectomy (Table II)

Total hysterectomy was performed as the primary procedure in 277 (38,4%) patients. This operation was suggested as definitive treatment after taking into consideration the patients' age, parity, desire for further pregnancies and the presence of additional lesions such as fibroids, endometriosis or menstrual abnormalities. While this may be considered a radical approach to the treatment of CIN, an additional and very important factor was the difficulty encountered in following up the population served. Adequate follow-up is considered imperative when conservative methods of treatment are more widely used.

In addition, hysterectomy was performed in 19 (2,6%) patients after initial cone biopsy, and in 10 patients (1,4%) after initial cryosurgery. A total of 306 patients (42,4%) were treated by total hysterectomy. There has been no recurrence so far in patients treated in this way.

Treatment by cone biopsy

Table III shows that therapeutic cone biopsy (TCB) was the primary treatment in 138 (19,1%) patients, none of whom required any further treatment. TCB was repeated in 5 patients

(0,7%); a further 10 patients (1,4%) required cryosurgery to eradicate the remaining lesion, and 9 patients (1,2%) required a total hysterectomy. Therefore, after therapeutic cone biopsy the disease recurred in 24 (14,8%) of the 162 patients who underwent therapeutic cone biopsy. All but 1 of the patients have remained free of disease at follow-up.

Diagnostic cone biopsy was performed in 42 patients. Twenty-two of these were subsequently treated by cryosurgery (52%) and 10 by total hysterectomy (24%). Where there was invasive carcinoma, either radical hysterectomy or radiation was used (10 patients, 24%). Therefore, in 32 patients (76%) with CIN the diagnostic cone biopsy was not therapeutic.

Treatment by cryosurgery

The 'double-freeze' cryosurgical technique was used (two 3-minute applications with an interval of 2 minutes).

As can be seen from Table IV, a single treatment was successful in 97 of 133 patients (72,9%) while cryosurgery had to be repeated to achieve cytological and colposcopic normality in a further 12 patients (9,0%). The overall success rate was thus 82%. In 24 patients (3,3%) additional treatment was necessary, 14 requiring a therapeutic cone biopsy and 10 a total hysterectomy for persistent disease.

The overall success rate of 82% is satisfactory, but it must be emphasized that only in exceptional circumstances were patients with CIN III treated in this way. With few exceptions only, CIN I and II (mild and moderate dysplasia) were treated by cryosurgery.

Discussion

CIN represents a unique situation in many ways: early diagnosis is common because of the widespread use of cytological examination of the cervix, the disease is occurring in younger women with increasing frequency, and, perhaps most importantly, there is no risk of lymphatic spread. Because of the latter factor complete local excision or destruction of the abnormal area is adequate treatment, provided that good follow-up is possible and

TABLE II. TREATMENT BY TOTAL HYSTERECTOMY

	No.	% of hysterectomies	% of total procedures
Total hysterectomy (vaginal and abdominal — primary)	277	90,5	38,4
Diagnostic cone biopsy, followed by hysterectomy	10	3,3	1,4
Therapeutic cone biopsy followed by hysterectomy	9	2,9	1,2
Cryosurgery followed by hysterectomy	10	3,3	1,4
Total	306	100,0	42,4

TABLE III. TREATMENT BY CONE BIOPSY

	No.	% of cone biopsies	% of total procedures
Therapeutic cone biopsy (TCB)	138	67,6	19,1
Repeat TCB	5	2,5	0,7
TCB followed by cryosurgery	10	4,9	1,4
TCB followed by total hysterectomy	9	4,4	1,2
Diagnostic cone biopsy	42	20,6	5,8
Followed by cryosurgery	22	10,8	3,1
Followed by total hysterectomy	10	4,9	1,4
Followed by radical hysterectomy	10	4,9	1,4
Total	204	100,0	28,2

TABLE IV. TREATMENT BY CRYOSURGERY

	No.	% of cryosurgical procedure	% of total procedures
Normal findings	97	72,9	13,4
Persistently positive: repeat cryosurgery	12	9,0	1,7
Persistently positive: TCB	14	10,5	1,9
Persistently positive: total hysterectomy	10	7,6	1,4
Total	133	100,0	18,4

that the entire lesion can be seen. Extension of the abnormal area into the endocervical canal, which cannot be evaluated colposcopically, absolutely contraindicates the use of local destructive therapy.

In this study total hysterectomy was the favoured form of treatment in 42,4% of patients, and the major reason for this policy decision, which would be considered radical in many developed countries, is the difficulty experienced with follow-up in the population groups served. It is striking that not a single vaginal vault recurrence has been documented, and this is attributed to the fact that in the 4% of patients in whom the CIN extended to the vaginal vault this was documented and the hysterectomy planned to include excision of a large enough cuff of vagina to ensure complete removal of the entire diseased area.

The types of locally destructive therapy available include cryosurgery, with a failure rate of approximately 18,7%,³⁻⁵ using the double-freeze technique. However, our own results and those of others^{6,7} have not been as good, with failure rates of 24,0% and 46,2%. In the present study cytonegativity was achieved in 82% of patients treated by cryosurgery, but it must be stressed that only minor degrees of CIN were managed in this way.

Using electrodiathermy and electrocautery success rates of 92% and 89% have been attained,⁸⁻¹¹ and the carbon dioxide laser appears to have come of age in the past 2 years,¹² with success rates of 94% reported in 1981 (J. A. Jordan — unpublished data). With the latter method the depth of tissue destruction should be 7 mm in order to ensure that abnormal epithelium deep in the cervical gland crypts is eliminated. This method of treatment has the additional advantages of pin-point accuracy, minimal offensive vaginal discharge after treatment and very little anatomical distortion of the cervix with good subsequent visibility of the squamocolumnar junction. The carbon dioxide laser is being used with increasing frequency in other gynaecological areas, e.g. for vulval and vaginal intra-epithelial neoplasia and surgery for infertility and endometriosis; the expense of the apparatus may well be offset by its extended application. This being so, it would appear to offer advantages over the other methods mentioned above.

No doubt other methods of local destructive treatment will be used for many years; provided the principles of therapy are strictly observed, good results will follow for the individual surgeon using the method with which he has experience and is comfortable.

The distinction between therapeutic and diagnostic cone biopsy may be thought to be artificial because the aim of the operation should always be total excision of the abnormal area. However, this distinction enables one to categorize those patients in whom a final diagnosis is possible only after histological examination of the cone biopsy specimen. Whereas the histological examination of a diagnostic cone biopsy sample will dictate the form of treatment, in the case of therapeutic cone biopsy

treatment will be determined by the cytological and histological findings of the directed colposcopic biopsy, provided that the full extent of the abnormal area can be viewed and there is no endocervical extension.

Therapeutic cone biopsy was followed by recurrence of disease in 14,8% of patients. In 94% of instances the abnormal area not excised was located at the endocervical excision line, which underlines the importance of identifying the internal os as an integral part of the technique in this operative procedure. In addition, 76% of the patients who were subjected to a diagnostic cone biopsy initially required additional treatment; this again emphasizes the fact that a cone biopsy of either type should not be performed by inexperienced gynaecological surgeons. The technique used at Groote Schuur Hospital involves the use of the colposcope or Lugol's iodine in the operating theatre in order to place the ectocervical excision line so that the abnormal area is completely excised on the ectocervix, the insertion of 2 lateral sutures at 3 and 9 o'clock, the identification of the internal os with a Hegar dilator, and the excision of a cervical cone from the external incision line to immediately below the internal os with a scalpel. Individual bleeding points are cauterized or occasionally sutured, and a vaginal plug is inserted for 24 hours. This technique has proved satisfactory and obviates the risk of concealing and burying residual abnormal epithelium.

The fact that no recurrence of disease occurred in the cervical vault and that vaginal recurrence has occurred in only 1 patient as yet is encouraging; we feel that the scheme of management is adequate for our particular circumstances.

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