Original Article

Cost-Effectiveness of Active versus Conservative Colposcopic Management of Mild Dyskaryosis

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Abstract: Management of mild dyskaryosis remains controversial. In this study, we compared the cost-effectiveness of active versus conservative colposcopic management of women presenting with mild dyskaryosis in two different hospital settings. All women presenting in 2001 with a mild dyskaryotic smear and requiring colposcopy were studied in two different clinical settings (70 women at Darent Valley Hospital (DVH) and 327 at St George’s Hospital (SGH)). At DVH, treatment is offered should there be any evidence of cervical intraepithelial neoplasia (CIN). On the other hand, a more conservative approach of cytological and colposcopic follow-up is offered to patients with evidence of low-grade disease at SGH. The outcome of both groups of patients was determined in terms of the number of colposcopy visits per patient, the risk of missing disease as a consequence of patients lost to follow-up and hospital costs as well as costs to patient over a four-year period. The majority (70%) of DVH patients had 1-2 colposcopy visits whereas the majority (60%) of SGH patients had 3-7 visits. At SGH 44% of untreated patients were lost to follow-up and an unknown number of those might have had high-grade disease. Active management is more cost-effective compared with conservative management (£323 and £589 as cost per patient effectively treated in the two hospitals respectively). In conclusion, active management of low-grade disease is associated with lower hospital and patient costs compared with the conservative strategy.

Key Words: Mild dyskaryosis, dysplasia, management, colposcopy, cost-effectiveness

Introduction

The management dilemma of the mildly dyskaryotic smear continues. First, the debate centred on cytological surveillance versus prompt referral for colposcopy. Those who advocate immediate colposcopic referral for mild dyskaryosis have supported their argument by cross-sectional studies showing that almost one-third of women with mild dyskaryotic smears have cervical intraepithelial neoplasia (CIN) 3 [1-3]. In addition, about 70% of women having cytological surveillance for mild dyskaryosis would ultimately be referred for colposcopy either because of unresolved low-grade abnormalities [4] or as a result of patient or doctor request. Consequently, the guidelines changed so that ideally, women with one mild dyskaryotic smear would be referred for colposcopy [5]. These changes have now opened a new debate about active versus conservative colposcopic management of low-grade disease. Following colposcopic assessment, low-grade disease may be treated there and then (active management) or followed up cytologically and colposcopically aiming for spontaneous regression (conservative management).

In today’s health care environment, with emphasis on the appropriate use of resources, it would appear that cost-effectiveness is nearly as important as clinical effectiveness. This study was conducted to compare the cost-effectiveness of two different management modalities (active versus conservative) for low-grade CIN in two different hospitals over a period of four years.

Materials and Methods

Women were recruited from the colposcopy clinics at Darent Valley Hospital (DVH, District General Hospital) in Kent and St. George’s Hospital (SGH, Teaching Hospital) in London.
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At DVH, an active approach is adopted for the management of mild dyskaryosis (Figure 1). On the other hand, a more conservative approach is in place at SGH for the management of mild dyskaryosis (Figure 2). The records of all women presenting in 2001 with a mildly dyskaryotic smear at the two hospitals were analysed over a four-year period (70 cases from DVH and 327 from SGH). There were only two cases with missing data (one from each hospital). The study examined the number of colposcopy visits per patient, clinical outcomes, hospital costs and costs to patients in the two groups.

**Results**

A total of 144 visits were made by the 69 patients at DVH, whereas a total of 990 visits were made by the 326 patients at SGH over the study period. The difference was 0.95 (95% CI 0.5 – 1.4) visits per patient and at SGH there were 45.6% (95% CI 24 – 67%) more visits per patient than at DVH.

The frequency of colposcopy visit to the two hospitals also differed. At SGH, about 60% of patients had 3-7 visits and 40% had 1-2 visits. While at DVH, about 70% of patients had 1-2 visits and only about 30% had 3-7 visits. The colposcopic findings in both hospital settings showed no significant difference (Table 1).

Hospital costs including colposcopy, treatment (large loop excision of transformation zone or LEETZ, cold coagulation, etc), histology, non-attendance of patients and smear taking were all quoted from previously published estimates [6-8] (Table 2). Costs to patients include the costs borne by women themselves due to travel, sick leave and child care.

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**Table 1** Summary of diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>DVH</th>
<th>SGH</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN2/CIN3</td>
<td>19 (27.5%)</td>
<td>66 (20.3%)</td>
</tr>
<tr>
<td>CIN1</td>
<td>36 (52.2%)</td>
<td>154 (47.2%)</td>
</tr>
<tr>
<td>No visible disease</td>
<td>8 (11.6%)</td>
<td>72 (22.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (8.7%)</td>
<td>34 (10.4%)</td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasia

**Table 2** Hospital visit and patient costs

<table>
<thead>
<tr>
<th></th>
<th>Hospital</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colposcopy</td>
<td>£100</td>
<td>£100</td>
</tr>
<tr>
<td>LLETZ etc</td>
<td>£40</td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td>£45</td>
<td></td>
</tr>
<tr>
<td>DNA</td>
<td>£100</td>
<td></td>
</tr>
<tr>
<td>Smear</td>
<td>£20</td>
<td></td>
</tr>
</tbody>
</table>

LLETZ, large loop excision of transformation zone (equivalent to LEEP)
Figure 2 Management flowchart for patients with mild dyskaryosis at SGH.

The hospital costs per patient as well as the costs to the patient were calculated at each hospital. As shown in Table 3, the hospital cost per patient at SGH was £466 compared with £323 at DVH. The cost to the patient was also higher at SGH than DVH. The purpose of the colposcopic management of CIN1 is to prevent the progress of the disease to CIN2 or higher. When patients default, their management cannot be considered to be effective. Consequently, the cost-effectiveness analysis must exclude these patients as their management has not been effective. It can therefore be concluded that the cost of effective management at DVH is £323 since no patient defaulted, whereas at SGH it was £589 (i.e. £152035/326 – 68). Furthermore, we followed up the 154 patients at SGH with initial diagnosis of CIN1 (Table 4). 5 of these patients (i.e. 3%, 95% CI = 1-7%) had follow-up
biopsies showing CIN2 or CIN3. These patients could have defaulted their colposcopy follow-up.

68 patients (44%) who were untreated did not attend their follow-up colposcopy. On the other hand, 32 patients (21%) who were followed up recovered without treatment. If the defaulted patients are excluded from the calculation, 37% of patients with effective management recovered without treatment. Finally, 49 patients (32%) had persistent CIN1 and received treatment.

Discussion

The ultimate objective of cervical cancer screening is to reduce deaths from cervical cancer by detecting and treating CIN. CIN has arbitrarily been divided into three categories (1, 2 and 3) [9] and recently a revised classification of high and low-grade lesions has been suggested [10].

The consensus is that high-grade lesions should be treated once diagnosed as they are likely to be cancer precursors [11]. On the other hand, the management of low-grade lesions still eludes a consensus of opinion as their natural history is poorly understood and they are associated with uncertain cancer potential [12].

The two treatment options of low-grade lesions are either immediate treatment once diagnosed or deferred treatment if they do not resolve after an initial period of surveillance usually two years.

In a prospective randomised trial, Flannely and co-workers [4] reported a 15% regression rate of all women with mild dyskaryosis, mostly in those women with CIN1 or HPV changes alone. Although these data supports a conservative approach, the safety and effectiveness of that approach depend on patient compliance.

In another prospective randomised trial by Shafi et al [13], 353 women younger than 35 years of age with mild dyskaryosis or borderline nuclear changes and adequate colposcopic examination were randomised to either immediate treatment by LLETZ or 24 months of cytological and colposcopic surveillance followed by LLETZ. They concluded that immediate referral and a select-and-treat management strategy is recommended based on one case of invasive cervical cancer, high default rate and the failure of cytology to pick up two cases of CIN3.

These two trials [4, 13] indicate that a conservative approach allows resolution of low-grade CIN and koilocytic atypia, but both had default rates of around 20% and the outcome for these women is unknown.

An important factor that is often neglected in the management of low-grade disease is the psychological state of the patient. A case-control study [14] comparing women undergoing surveillance for mild dyskaryosis with women referred for colposcopy found that the initial anxiety in women undergoing surveillance is less than that in women referred for colposcopy but, following colposcopy, anxiety is rapidly resolved while elevated anxiety persists in women under surveillance due to the length of period of protracted abnormality.

So far, there are no economic data specifically related to the management of women with low-grade lesions. One study looked at the cost of detecting high-grade disease in women with mild dyskaryosis when promptly referred for colposcopy [7].

Our study looked at a direct comparison of immediate versus deferred treatment of low-grade disease in terms of the number of colposcopy visits, hospital costs, and costs to
patient as well as the risk of missing disease as a consequence of patients lost to follow-up.

The benefits of the active management policy compared with the conservative policy are lower hospital and patient costs, reduced patient anxiety due to protracted abnormality and a smaller risk of CIN1 progressing in untreated patients lost to follow-up. In addition, treating all CIN1 immediately can be expected to prevent more serious disease developing in 3% of patients and persistent disease remaining in 32% of them.

On the other hand, 21% or more of patients who received immediate treatment (LLETZ or cold coagulation) for CIN1 at DVH might be expected to resolve without treatment. HPV testing might help select high-risk women with low-grade disease for treatment. Low-grade diseases with high-risk HPV types are more likely to persist or progress [15]. Hence HPV testing may be useful in identifying women who can avoid both unnecessary treatment and excessive surveillance.

The use of ‘Select and Treat’ rather than ‘See and Treat’ policy might reduce the risk of over treatment associated with the immediate treatment of low-grade smear abnormalities [13]. Obviously, this depends on the expertise of the colposcopist examining the patient. The multivisit deferred treatment strategy for low-grade disease is time-consuming, costly and anxiety-provoking for patients.

The data available on the management of women with CIN1 is still insufficient to advocate a single strategy and, while this demands further research, it should also prompt us to involve our patients in deciding on the best option for them. In other words, until data is available, we suggest that the patient herself should choose which strategy she would like to follow. Active management of low-grade disease is associated with lower hospital and patient costs compared with the conservative policy.

References

[14] Falls RK. Spontaneous resolution rate of grade 1 cervical intra-epithelial neoplasia in a private