Normal colposcopy following abnormal Pap smear evoking LGSIL: A follow-up study

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Summary

The aim of this study was to determine the optimal treatment policy in women presenting with an abnormal Pap smear showing low-grade squamous intraepithelial lesion (LGSIL), who additionally had normal colposcopic findings. We prospectively studied 160 women with LGSIL and normal colposcopy, and divided them into two groups. Group A, consisting of 54 women, was followed-up for a mean period of 42 months and had a new control smear 12 months after the initial one. Group B, consisting of 106 women, was followed-up for a mean period of 44 months and had two consecutive control smears (6 and 12 months after the initial), and a new colposcopy, depending on the findings.

At the end of the first year, the lesion persisted in 37% and 39% of the patients in groups A and B, respectively. At the end of the study, regression or persistence of the LGSIL was revealed in 63% and 61% of the women in groups A and B, respectively. Aggravation of the lesions occurred after 16.5 and 15 months, respectively, in groups A and B.

Our findings suggest that women with LGSIL and normal colposcopy do not need further therapeutic measures during the first year after the initial smear.

Key words: LGSIL; Colposcopy; Follow-up.

Introduction

It is well documented that although cervical cancer remains one of the commonest cancers in women, it can be prevented and usually it can be cured. In the USA there has been a 70% decline in mortality rates from cervical cancer in the last 50 years. This is mainly attributed to mass screening, implementing the Pap smear for early diagnosis of preinvasive malignancies of the cervical epithelium.

According to the Bethesda system, intraepithelial lesions of the squamous epithelium of the cervix are graded as low (LGSIL) and high (HGSIL). In patients where the Pap smear reveals HGSIL, the next step to establish the diagnosis and determine the following therapeutic measures, are colposcopy and biopsy sampling. Moreover, thousands of women with LGSIL are screened each year by Pap smears. A wide range (4%-64%) of colposcopies performed within a six-month span from the initial smear (showing cytologic findings implying LGSIL) are actually proven to be normal [1].

The aim of the study was to determine the management of women presenting with LGSIL cytologic findings who showed a normal-appearing cervix on colposcopy.

Patients and Methods

We studied 494 women aged 18-47 years (median age 29 years) diagnosed as having LGSILs. These patients underwent colposcopy, performed by a colposcopy specialist, which appeared normal in 202 of the patients (fully visible and normal-looking transformation zone). All colposcopic images were stored in a database, re-estimated by another gynecologist who ignored the initial diagnosis, and then were randomly compared using an archive of normal colposcopic exams. Post re-examination, a colposcopic image of a fully visible and normal appearing transformation zone was confirmed in 181 cases, 160 of which were further selected, under the following criteria:

1. No concurrent gestation was present.
2. Contraceptive modality was declared.
3. Data concerning smoking status were available.
4. No pre-existent Pap smear implying more severe lesions than the one citing LGSIL was stated.
5. The exact date (phase within the cycle) of receiving the Pap smear revealing LGSIL was known.
6. The patient had to be capable of participating in the required follow-up.
7. The cytologic findings of the specimen complied with the following fixed criteria:

i. Nuclear magnification, at least three times the size of a normal nucleus;

ii. A moderate change in the nuclear shape, and/or dense chromatin, and/or double nuclei;

iii. The presence of coilocytosis was not taken into account to establish the diagnosis.

Based on epidemiological data, and accepting the colposcopic diagnosis as correct, those women were divided into two groups that were studied prospectively.

The first group consisted of 54 women who underwent a repeat cytologic exam 12 months after the initial one, without any additional follow-up during that period. These patients were informed by their gynecologist about the possibility of remission or progression to more severe lesions. Smokers were advised to quit smoking, and women who rarely or never used condoms were advised to use them or to abstain for several months. The mean period of follow-up for patients in the first group was 42 months.

Revised manuscript accepted for publication April 6, 2004

The second group consisted of 106 women in whom two cytologic exams (6 and 12 months after the initial one) were performed as well as a new colposcopic evaluation upon the findings of the cytologic exams. The same advice about smoking and condom use was provided. The mean length of follow-up for women in the second group was 44 months.

Results

At the end of the first year of follow-up similar cytologic findings without signs of remission were present in 37% of the patients in the first group and in 39% of those in the second (not statistically significant, $p > 0.5$). Of these, 85% of the first group and 80% of the second did not quit smoking, and 79% and 82%, respectively, did not use condoms.

At the end of the survey, remission/persistence of cytologic findings was revealed in 34/54 (~63%) of the patients in the first group and in 65/106 (~61%) in the second. It should be noted that 96% of the women in the first group and 97% in the second stopped smoking, while 87% and 82%, respectively, were condom users.

Aggravation of the cytologic findings was established 16.5 months after the initial smear for the patients in the first group, and 15 months after for the second group, respectively.

Discussion

The results of our study show that 37% of the patients in the first group and 39% in the second presented deterioration of the LGSIL cervical lesions during the follow-up period. These findings – implying similarity of outcome between the two subgroups – comply with the results of Anderson *et al.* [2], who followed-up 53 women with LGSILs for a 7-month period, and revealed progressive cytologic findings in 31% of them.

Hellberg *et al.* [3], followed-up 328 women with HGSIL and normal colposcopy for a ten-year period. At the end of the first year, 22% of the patients showed some progression of cytologic findings. Milne *et al.* [4] followed-up 120 women with LGSILs and normal colposcopy for a period of five years, and found progression of the cytologic findings in 38% of patients.

In our study no statistically significant difference ($p > 0.5$) was observed concerning the persistence/progression of cytologic findings between the two groups of patients at the end of the first year of follow-up. Smoking and condom use did seem to play an important role in both groups of patients who showed remission/persistence of LGSILs.

In addition a statistically significant difference ($p > 0.5$) concerning the length of time between initial LGSIL diagnosis and progression of the lesions between the two groups was not found.

In spite of methodological problems in the statistical analysis, originating from the unequal number of patients and follow-up periods, the results imply that in women presenting with minor cytologic lesions and a normal-appearing cervix at colposcopy, a less invasive policy during the first year after the initial diagnosis even without further examination is relatively safe.

Concerning the potential role of large loop excision of the transformation zone (LLETZ), we would agree with Roland *et al.* who believe that abandonment of colposcopy and reliance on immediate LLETZ may be expensive and have significant potential for excessive treatment, concluding that traditional colposcopic evaluation coupled with observation of mild dysplasia is the most cost-effective means of treating cervical dysplasia and has a low potential for excessive treatment [5].

Among others, Lonky *et al.* [6] question the role of Pap smears, citing that a single Pap smear might have a false negative rate to detect dysplasia as high as 65%, making cytology an inaccurate diagnostic replacemant for colposcopy. The points made by Mannino *et al.* [7], Meanec *et al.* [8], and Mayeux *et al.* [10] are similar.

Despite the fact that evaluation and treatment of abnormal Pap smears citing SIL remain an area of conflict, as demonstrated in the literature, it should be kept in mind that upon diagnosis of an intraepithelial lesion, the reliability of a Pap smear ranges between 70-80%, while colposcopy sensitivity may be as high as 96% [10].

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