Regression rate of clinical HPV infection of the lower genital tract during pregnancy after laser CO₂ surgery

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Summary

The objective of the study was to evaluate the effects of laser CO₂ surgery during pregnancy to prevent clinical HPV infection recurrence after delivery and vertical infection.

A case-control study was performed on 280 pregnant women affected by clinical HPV infection treated during pregnancy with 256 women treated three months after delivery. Follow-up was performed for a minimum of three colposcopic examinations for two years. Recurrence rates were calculated considering the number of positive findings for at least one colposcopic examination confirmed by biopsy after a negative control in a year. Statistical comparison of rates was performed by χ² and Fisher’s exact test. Recurrence rates were higher in the women treated in postpartum (p < .01) than in the group treated during gestation (p < .005).

Clinical HPV infections treated during the second trimester of pregnancy showed a sensitive decrease in recurrence rate of infection. Rarity of respiratory papillomatosis makes conclusions inconsistent for the prevention of vertical infection.

Key words: Pregnancy; HPV; Laser CO₂.

Introduction

HPV is currently the most widespread infection in the world and its prevalence is estimated differently in the literature, varying from 10% to 60%; this range, even though unexpectedly broad, can be explained if we take into account the great number of diagnostic techniques employed [1-3].

From more than 100 HPV types currently known, some are considered highly oncogenic, whereas others seem to be less pathogenic in that they show a less marked tendency to produce lesions that can lead to neoplastic degeneration [4].

There are reasons to believe that pregnancy, because of the modifications of the immunological and hormonal environment that characterize it, favor an increased incidence of infections from HPV and HPV-linked lesions. On the other hand it can cause the progression of dysplastic disease towards more evidently carcinomatous forms [5-8].

Another factor that justifies the interest demonstrated by the medical and scientific community regarding the relationship between HPV and pregnancy is given by the possibility, almost unanimously accepted, of a maternal-fetal transmission of the virus with the related risk for the newborn of developing juvenile laryngeal papillomatosis (JLP - a disease in which papillomas of the larynx and upper respiratory tract cause hoarseness and respiratory obstruction). Estimates for JLP are similarly imprecise, with incidence rates of 0.4 to 1.2 per 100,000 children [7, 9]. Types most frequently involved in JLP are HPV 6 and HPV 11, both among the most commonly observed at the genital level. Furthermore, it has been shown that HPV-positive children born from similarly infected HPV/DNA-positive women, present at the buccal level the same variants of papillomavirus detected in the cervixes of their mothers [10].

The currently estimated risk of perinatal transmission is about 50% [11] and anal-genital lesions diagnosed within the first year of life can be considered as acquired perinatally [11-13].

Thus, the combination of the malignant potential of HPV, its high prevalence of infection and the relative diminished gestational immuno-responsiveness confers the importance of generalized clinical and virological significance during pregnancy, in postpartum and pediatric care.

Factors such as pregnancy hormones and diminished immune responsiveness may promote the growth of cervical and vulvovaginal HPV-induced lesions that make complex colposcopic findings needed.

Laser CO₂ vaporization/excision for vulvovaginal warts during gestation is well documented as safe for the mother and fetus with no increased risk of pregnancy complications or preterm birth [14-16].

The objective of the study was to assess the effects of laser CO₂ vaporization/excision to prevent clinical HPV infection recurrence after delivery and the rate of vertical transmission.

Material and Methods

We performed a randomized case-control study comparing 280 pregnant women with clinical HPV infection treated during the second trimester of pregnancy with 256 women treated three months after delivery. Follow-up was carried out with a
minimum of three colposcopic examinations during gestation
and for two years after delivery. Recurrence rates were calculated
considering the number of positive findings for at least
one colposcopic control confirmed by biopsy after one negative
control in year. HPV-DNA testing was not performed. All
patients affected by HPv infections underwent biopsy. Patients
were submitted to laser CO₂ vaporization/excision during the
second trimester from one to three steps. Exclusion criteria
were spontaneous regression of condylomatoses or aceto white
lesions without confirmed biopsy. Histologic diagnosis was pro-
vided according to the classification proposed by the Interna-
tional Society for the Study of Vulvar Disease. A colposcopic
examination was carried out in all patients to rule out the pres-
ence of cervical HPV infections or a squamous intraepithelial
lesion (SIL). Treatments were performed under local anes-
thesia. A Zeiss CO₂ laser attached to a Zeiss T 50 coloscope was
used, in continuous mode with a power density ranging between
600 and 1200 W/cm². Power densities above 1,000 W/cm² were
used for lesion vaporization, whereas lower power densities
were used at the periphery of the excised tissue or to coagulate
slight bleeding; the smallest spot size was 0.5 mm. All pro-
cedures were performed under colposcopic guidance, with a local
length of 300 mm, after the application of 5% acetic acid. Two
weeks later, in the presence of persistent HPV lesions, the
patients were submitted again to laser CO₂ surgery.

The first follow-up was performed four weeks after the
procedure and subsequently at six months. Data demographic
anamnestic characteristics, size and location of the lesions and
follow-up was recorded in our database. HIV-seropositive
patients were excluded from the study. Chart reviews of our uni-
versity hospital medical records from the ear, nose and throat
pediatric department were used to identify the cases of res-
piratory papillomatosis due to vertical infection.

Statistical comparison of rates was performed by the chi-
square and Fisher's exact test.

Results

A total of 536 pregnant women with external genital
warts were treated between 1998 and 2001. 280 during
the second trimester, and 256 within a minimum of three
months after delivery. There were 440 vulvar lesions, 43
anoperineal, 80 vaginal and 90 cervical. Two hundred
and thirty-two patients needed a second treatment, 40 needed
a third and four patients a fourth. In the follow-up three
months after delivery in the first group none needed treat-
ment. After six months 14 patients were submitted to a
second treatment (8 patients had vulvar lesions and 6
patients had cervical lesions) and 12 months after eight
patients (4 patients with vulvar lesions and 4 patients
with cervical lesions) needed a third treatment; 13 pro-
cedures had to be suspended due to increased blood loss
and seven for patient non compliance.

In the second group, until the end of the second
trimester and during the third trimester 10.5% (27/256) of
the HPV lesions were still growing in size; 66.5%
(170/256) were stationary while 23% (59/256) had
diminished. Gestational age at delivery in the two groups
was 36 ± 2 vs 37 ± 3 weeks and the birthweight was
3,467 ± 300 vs 3,360 ± 282 g, respectively (Table 1).

Recurrence rates were higher in the women treated
post-partum (7.9 ± 1.4 vs 4.3 ± 0.9; p < 01) than in the

<table>
<thead>
<tr>
<th>Table 1. — Pregnancy outcome and distribution of lesions.</th>
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<tbody>
<tr>
<td>Clinical HPV infection (n = 536)</td>
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<tr>
<td>Cervical HPV  (n = 90)</td>
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<tr>
<td>Cesarean section</td>
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| Table 2. — Variation of HPv+ fetuses at birth in relation to the
interval between the breaking of membranes and the end of
delivery [10]. |
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<tbody>
<tr>
<td>Interval (hr)</td>
<td>Fetuses HPv+</td>
<td>%</td>
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<tr>
<td>2</td>
<td>11</td>
<td>0</td>
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<td>2-4</td>
<td>21</td>
<td>7</td>
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Estimates for genital warts are less precise than those
for cancer because of the absence of case reporting and
because they often recur after treatment, however, limited
data suggest that in the U.S. incidence rates may be as
high as 100 per 100,000 [17] with a prevalence of 1.4
million [18].

Identification of HPV types 6 and 11 from both genital
warts and respiratory papillomatosis provided evidence for
the etiological link between vulvo-vaginal condyloma and
JLP [9].

The risk of vertical transmission is linked to the fol-
lowing factors: delivery by the vaginal route [12, 19],
maternal viral load [20-22], the time elapsing between
the breaking of membranes and the end of delivery in
single cases [10] (Table 2).

On the basis of the above considerations, we believe it
is important to remove condylomatous lesions at the
maternal genital level before women give birth.

However, genital papillomatosis does not seem to
require an elective cesarean section because this practice
does not bring about important advantages from the point
of view of the cost/benefit ratio.

Vaccines still need to be proven to be effective, espe-
cially during pregnancy. The imiquimod derivative
(Aldara) that induces macrophages to secrete cytokines
(IL-2 and INF-α) is applied topically; a 5% preparation
is more efficacious and has been approved by the US
Food and Drug Administration in non pregnant women
whereas safety during gestation has not been tested.

The relative safety and effectiveness of surgical treat-
ment show that this “overtreatment” results in a signifi-
cant decrease in recurrence. Among all therapeutic

Discussion

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options laser CO₂ surgery has proven efficacy and only rarely do side-effects or important complications occur. Consequently it could be a suitable and effective treatment during gestation. It is well documented as safe for the mother and fetus with no increased risk of pregnancy complications or pre-term birth [14-16]. As a preventive approach for newborn vertical infections results did not reach statistical significance, although the results apparently indicate that in treatment during the second trimester it is protective; while all of the children affected by JLP mothers had cervicovaginal infections, the relative rarity of the pathology needs a larger number of cases to reach a definitive conclusion.

References


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