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Research Article

Colposcopic-Magnified Scan-Aided CO2 Laser Vaporization for Genital Warts in Pregnancy: a Propsective Descriptive Evaluation of Safety in a Tertiary Care Obstetrical Hospital

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Abstract

Objectives: Genital warts caused by infection with LOW RISK HPV may infect newborns risking to develop Juvenile Onset Recurrent Respiratory Papillomatosis (JORRP). No clear guidelines are available to manage genital warts in pregnancy. Although cesarean section is not recommended, almost 20% of warty pregnant patients still undergo cesarean section due to genital warts in labour. Aim was to show efficiency of a minimally invasive laser technique to treat warts in pregnancy.

Methods: A prospective study on all patients of Authors' obstetrical ward diagnosed from 2014 to 2019 with genital warts during pregnancy and submitted to Colposcopic Magnified Scan-aided CO_2 Laser Vaporization (CMSLV) was conducted. The aim of every laser session was no residual disease. Patients were submitted to colposcopy every three weeks until delivery to assess and treat eventual relapse. Laser outcome was evaluated in term of number of treatments per pregnancy. Rates of preterm labour, cesarean section and indication to cesarean section, performed episiotomy, occurred perineal tears were collected and compared to rates of the obstetrical population delivering at Authors' clinic in 2021.Rate of breastfeeding was collected as index of mother wellbeing. Infants were followed for three years after birth at neonatologic unit to check for JORRP.

Results: 221 pregnant women were enrolled: 29.8 % needed multiple-site laser vaporization, 86% needed a singular procedure, while 14% multiple treatments. 8.1% cesarean section were performed but only 0.9% because of genital warts. No statistically difference in term of obstetrical outcomes were observed among patients who underwent single or multiple procedures. CMSLV didn't represent a major risk factor for cesarean section or operative procedures when compared to a third level care unit population risk factors). 78.3% of newborns were exclusively breastfed. No JORRP cases were registered among the case series' infants.

Conclusions: CMSLV minimizes vaporized areas, can be performed in outpatient setting with local anesthesia up to the term of gestation, reduces the risk of chosing cesarean section as JORRP preventing option under 1% and preserves obstetrical outcomes and mothers'wellbeing.

Keywords: Cesarean section; Laser; Pregnancy; Wart

Introduction

Condyloma acuminata is a benign neoplasm that develops in the genital tract and it is caused by infection with Human Papillomavirus (HPV) types 6 and 11. In pregnant women, the lesions generally tend to grow rapidly. This may be because of changes in hormone levels, increased vaginal discharge and reduced immune responsiveness. Most infants are infected during vaginal birth, but also intrauterine infection can occur. This infection results in papillomas primarily in the larynx, vocal cords, epiglottis and oral pharynx which present during infancy or childhood requiring frequent surgery under general anesthesia to maintain an open airway. The multiple surgical procedures frequently cause scar tissue to impair the voice significantly. Juvenile Onset Recurrent Respiratory Papillomatosis (JORRP) is a non-malignant condition and as a result, guidelines do not strongly recommend caesarean section for the prevention of neonatal HPV infection. Besides this, almost 20% of warty pregnant patients still undergo caesarean section due to condyloma acuminata [1] since no clear guidelines are available for the management of pregnant women with condyloma acuminata which remain the main risk factor for the development of JORRP. Available treatment options are classified into patient-applied treatment and provider-applied treatment. The principal medication used on patient-applied treatment is imiquimod cream while multiple provider-applied treatments are described such as laser therapy, cryotherapy, photodynamic therapy, trichloroacetic acid and local hyperthermia. Author's aim was to show safety and reliability of a minimally invasive scan-aided laser CO_2 vaporization technique applied under colposcopic magnification in the management of warty pregnant patients assisted during the entire pregnancy and labor.

Materials and Methods

A prospective taking care study of all patients diagnosed from 2014 to 2019 with genital warts during pregnancy and submitted to Colposcopic Magnified Scan-aided CO_2 Laser Vaporization (CMSLV) at AOUC (Azienda Ospedaliero-Universitaria Careggi) Colposcopy and laser surgery unit was conducted. Only patients that were followed by our outpatient setting prenatal care unit and delivered at our obstetric inward were enrolled. Pregnancies with multiple records on overlapping dates and pregnancy records with implausible or missing information on gestational age were excluded. All vaporization procedures were performed with a SmartXide^2 C80 CO_2 laser (DEKA M.E.L.A. Srl) at 15 watts of power in CW mode and a dwell time of 0.1msec. in repeated mode of emission, using a scan aided microspot Micromanipulator, Easyspot, coupled with HiScan Surgical scanner (see Figure 1) and connected to a Zeiss 150-FC colposcope. The scanning shape was a filled hexagon tailored on warts' localization and dimension.

Figure 1: Microspot Micromanipulator, Easyspot, coupled with HiScan Surgical scanner.

Procedures were performed after applying EMLA cream (lidocaine 2.5% + prilocaine 2.5%), local injectable anesthetic (1:200000 optocain with adrenaline) was limited to EMLA not responding pain and wide procedures. A smoke evacuator was used during the procedures for reducing smoke exposure. The aim of every laser surgical session was no residual disease. Patients were submitted to colposcopy and vulvoscopy every three weeks until delivery to assess and treat eventual relapse. Surgical outcome was evaluated in term of relapsing rate during pregnancy and numbers of treatment per pregnancy. Rates of preterm labor, caesarean section and indication to caesarean section, performed episiotomy, occurred perineal tears were collected and compared to rates of the entire obstetrical population delivering at our clinic in 2021. Rate of breastfeeding reached in the treated population was collected as index of mother and child wellbeing and compared to AOUC BFH standard rate. Infants were followed for three years after birth from neonatal Care unit of AOUC Hospital to check for JORRP. Results were statistically analyzed by Chi Square test with Yates correction considering a $p<0,05$ as significative.

Results

From 2014 to 2019 231 pregnant women have been submitted at the Colposcopy and Laser Surgery Unit to CMSLV because of genital warts. Patients' mean of age was 32 (range 18-46). Among them 221 (95.5%) were followed by AOUC Prenatal Care Unit and delivered at Our Obstetrical Clinic while 10 (4.5%) experienced miscarriage within 20ws of gestation (range 6-18) and were excluded from the case series. 66 women/221 (29.9%) were submitted to multiple site laser vaporization (vulva+vagina/+vagina and cervix/+ cervix) but 163/ 232 (70.1%), the majority of them, where submitted only to vulvar laser procedures. 190/221 (86%) women were submitted to a singular laser procedure during the entire pregnancy while 14/221 (14%) patients experienced multiple treatments (5: 1 pt; 4: 1pt; 3:9pts; 2: 20pts), 18/221 (8.1%) of women were submitted to caesarean section and among

these only 2/221 (0.9%) performed a caesarean section because of genital warts during labor representing treatment failure.

9/203 (4%) of women experienced an operative delivery with the application of the vacuum extractor, 7/203 (3.4%) episiotomy and 16/203 (16.2%) a spontaneous perineal tear (lac I: 79% (26); lac II: 18% (6); lac III: 3% (1); lac IV: none). 41/221 (18.5%) women experienced a preterm labor and delivery. No statistically difference in term of preterm labor, caesarean section, operative delivery, episiotomy or spontaneous perineal tearing rates were observed among patient who underwent single or multiple laser procedures during pregnancy (Table 1).

	single laser treatment	multiple treatments	p<0.05
cesarean section	14/190	4/31	**n.s.**
vacuum extractor	8/190	1/31	**n.s.**
episiotomy	7/190	0/31	**n.s.**
perineal tears	28/190	5/31	**n.s.**

Table 1: Treatment failure/HPV persistence and obstetrical outcomes.

No JORRP cases were registered among the case series infants. HPV productive infection and its laser treatment did not represent a major risk factor for caesarean section or operative procedures when compared to a third level care unit population risk factors; more over laser treatment seemed to reduce the risk of perineal tears (Table 2). 78.3% (174/221) of newborns were exclusively breastfed. No JORRP cases were registered among the case series infants.

	2021 obstetrical population	laser treated population	p<0.05
cesarean section	797/2798 (28.5%)	18/221 (8.1%)	**p<0.003**
po	170 /2001(8.5%)	9/203(4.4%)	**n.s.**
episiotomy	139/2001 (6.9%)	7/203 (3.4%)	**n.s.**
perineal tears	1215/2001 (60.7%)	34/203 (16.7%)	**p< 0.0001**
preterm	314/2798 (11.2%)	6/221 (2.7%)	**p<0.00036**
twin	102/2798 (3.6%)	0/221	**p<0.001**
ivf	216/2798 (7.7%)	1 /221 (0.4%)	**p<0.0004**
multiparity	1365/2798 (48.8%)	46/221 (20.8%)	**p<0.001**

Table 2: Comparison to AOUC obstetrical population.

Discussion

CO_2 lasers have already been described in past literature presenting a good efficacy and low complication rate for the treatment of Human Papillomavirus (HPV) genital condyloma and verrucose carcinoma in pregnant females [2-4], mostly because CO_2 laser has a limited penetration into the skin with the added advantage of bloodless destruction due to coagulation property. Despite this, its use was limited through years because its application was derived from dermatological experience administering a lot of energy on widely spread areas so to require general or spinal anesthesia to make patients endure the heat [5]. Moreover, CO_2 laser treatments during pregnancy were hampered by obstetrical complications described in literature: Schwartz et al. reported a case of preterm premature rupture of membranes (PROMs) 4 days after laser therapy was performed at 35 weeks of gestation [6]; Hankins et al. reported a case of clinical chorioamnionitis with fever and uterine tenderness 8 hours after laser therapy at 36 weeks of gestation [7].

Since Ferenczy reported that the recurrence rate after CO_2 laser treatment of warts was high in the first trimester (33%) and decreased in the second trimester (17%) with no recurrences observed in the third trimester its use was also proposed to be limited to first and second trimester [8]. This limitation together with the fact that interferon, 5-fluorouracil cream, and cidofovir are not currently recommended sinecatechins, podophyllin resin, and podophyllotoxin should not be used in pregnant women [9] determined that criotherapy and imiquimod 5% were proposed as only alternative safe treatments [10]. Reported advantages of these self-applied treatments include the elimination of frequent outpatient visits, the possibility of using them during all the three trimesters, the unreported complications to fetuses, the mild complications experienced by mothers such as local erythema and low rate of not responding recurrence and requiring surgery [11,12]. Nevertheless, none of the reports can evaluate obstetrical outcomes since the small case series of the treated population.

Moreover, US Centers for Disease Control and Prevention does not recommend topical therapy with imiquimod in pregnancy [13]. The present manuscript is to Author's knowledge the largest case series of warty pregnant population prospectively followed during the entire pregnancy and delivery; its results show CMSLV performed up to the term of the pregnancy safe and reliable to reduce the risk of caesarean section for this indication under 1%, with no JORRP in the infants after three years from delivery. Therefore authors suggest that pregnant patients with warts should be followed by a tertiary care hospital where colposcopy and vulvoscopy can be performed during the entire pregnancy with the aim of no residual disease at the time of delivery. The colposcopic

magnification and illumination connected to CO_2 laser Scan-aided microspot Micromanipulator helps to limit the vaporized areas to the warts' basis, reducing the heat perceived by patients allowing the outpatient setting and patients' retention to treatment although in approximately 15% of women this needs to be repeated several times. This is in contrast with previous observation that described CO_2 laser treatments with no colposcopic magnification unable to treat extensive areas worrying patients [11]. The Scanning Micromanipulator is of the same generation and technology of those used nowadays in ENT or neurosurgical prodedures [14-15], the scanner fastly and precisely moves on the tissue a microspot of 250mm of diameter focused by the micromanipulators' zoom at 300mm EFL (the working distance of the colposcope) creating shapes suited for cutting and ablation: Hexagons, circles, lines. This allows to deliver the energy to the tissue controlling in a repeatable way depth of ablation and limiting the thermal damage.

Minimizing vaporized areas and reducing the thermal effect and the consequent pain allows procedures to be performed only using topical anesthesia and reserving Injectable local anesthetics to no-responder patients so to avoid potential risks due to fetal exposure to anesthetics such as central nervous system toxicity and neutrophil chemotaxis inhibition [16]. As previously observed for not pregnant and male patients [17] a major advantage of CMLSV is to allow the simultaneous treatment of multiple sites whether vulvar or vaginal reaching the lesion clearance in only one session. Literature reports that perineal tears may affect up to 80% of women during childbirth, with primiparous women being affected more frequently than multiparous women [18,19] data that are confirmed in the AOUC 2021 population which experienced a 60% of perineal trauma.

CMLSV treated women seemed to be protected from the risk of perineal tearing since only 18,5% of them had one of any degree. Possible explanation is to find into a deeper care reserved to genital tissues during labor and delivery by the hospital midwives and physicians aware of the treatments performed. CMLSV did not expose pregnant patients to a higher risk of preterm labor which rate was 2,75 % versus 10.1% of preterm newborns in AOUC 2021 obstetrical population in agreement with registered 2021 world rate and reported by Center of Diseases Control [20]. CMLSV seemed not to be detrimental on mothers' physical and mental health since 78% of them exclusively breastfed newborn, rate which is higher than the world median one which is reported to be 65% [21]. Similar advantages of CO_2 laser vaporization connected to colposcopic magnification are to be supposed when the same procedure is performed to other vulvar dermatological diseases during pregnancy such as molluscum, genital malformation as hymenal septum, infibulation, or bleeding cutaneous polyps. Authors presented initial scientific material on the theme to Eurogin 2023 congress in a poster session and used it to edit the present structured manuscript clarifying definitive advantages of the presented laser treatment. Words and ideas of the present manuscript were revised along with laser-tissue interaction skills of an added technical author to upgrade physicians' knowledge of laser's operating mechanism on organic tissue and implement their confidence [22].

Conclusion

Colposcopic-magnified Scan-aided CO_2 Laser Vaporization is a safe reliable outpatient therapy for genital warts during pregnancy. It allows to reduce the risk of choosing caesarean section as JORRP preventing option and it preserves obstetrical outcomes.

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