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Natalia Mayumi Inada, Cynthia Aparecida de Castro, Hilde Harb Buzzá, Wellington Lombardi, Vanderlei Salvador Bagnato, "Long-term effectiveness and HPV clearance of low and high-grade cervical lesions treated with photodynamic therapy," Proc. SPIE 11070, 17th International Photodynamic Association World Congress, 110706Z (7 August 2019); doi: 10.1117/12.2524706

SPIE.

Event: 17th International Photodynamic Association World Congress, 2019, Cambridge, Massachusetts, United States

11070-226



Long-term Effectiveness and HPV Clearance of Low and High-grade Cervical Lesions Treated with Photodynamic Therapy



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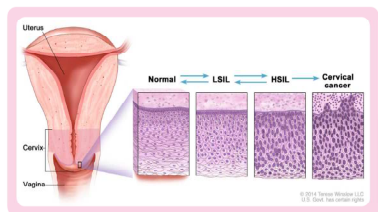
INTRODUCTION

Cervical cancer is the fourth most frequent cancer in women worldwide. For Brazil, there are estimated 16,370 new cases of cervical cancer for each year of the biennium of 2018-2019, with an estimated risk of 15.43 cases per 100,000 women, occupying the third position [1]. Persistent infection with Human papillomavirus (HPV) has been identified as the major cause of the Cervical Intraepithelial Neoplasia (CIN), a precursor of cervical cancer. The classification of CIN is based on the cellular features to discriminate dysplasia levels, being CIN 1 as mild dysplasia and CIN 2/3 as moderate or severe dysplasia [2]. Cervical cancer can be prevented with a early CIN diagnosis and treatment [3].

CERVICAL CANCER in BRAZIL
Estimated new cases: 16,370 (2018)
Mortality: 5,430 (2018)



This is a controlled non-randomized clinical trial for CIN 1, 2/3 treatment with photodynamic therapy. The follow up with colposcopy, Pap test, and biopsy in HSIL cases was performed at 30, 60, 90, 180 days, and at one and two years after PDT. CIN 1 (n = 70), CIN 2 (n = 10), CIN 3 (n = 10) and placebo group (n = 15) were treated with different protocols.



NIH Publication 14-5199. Understanding Cervical Changes: a health guide for women. Aug. 2014, p. 08.

METHODS

1. Patient enrollment

Fifty-six patients with CIN 1 were treated between April 2013 and October 2015, and monitored up to July 2017. A placebo group formed by 14 patients received only light (n=8) or only topical methyl aminolevulinate cream (n=6), with the same parameters for CIN 1 treatment, was followed also up to two years. Ten patients with CIN 2/3 were treated between April 2015 and September 2016, and monitored up to December 2018. Written informed consent was obtained following approval by the Human Medical Ethics Committee (CEP 827.010, April 2013).

2. MAL cream application

Patients were positioned in a gynecological bed and 2 g of cream containing 20% (w/w) of methyl aminolevulinate (MAL, PDTPharma, Cravinhos-SP, Brazil) was applied using a needleless syringe and a tampon was used to keep the cream in place for one hour for CIN 1 or placebo group, and three hours for CIN 2/3.

3. Photodynamic Therapy

CerCa 150 System® has a LED probe emitting at 630 nm and was delivered an irradiance of 80 mW/cm² for 21 minutes (100.8 J/cm²) for CIN 1 patients, and 120 mW/cm² for 25 minutes (180 J/cm²) for CIN 2/3 treatment. Only CIN 2/3 patients received two PDT application, one week apart. Sixty days after the second PDT, was performed a less profound Loop Electrosurgical Excision Procedure (LEEP) to remove part of the affected cervix for histopathological analysis.

4. Follow-up

The patients with CIN 1 were followed by 30 and 90 days after PDT, and by two other long-term follow-ups of 1 and 2 years after the treatment. The patients with CIN 2/3 were followed by 60 days after LEEP, and by two other long-term follow-ups of 1 and 2 years after the treatment. The clinical evaluation was performed by colposcopy, autofluorescence visualization and Pap test all the patients.

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RESULTS

No dysplasia was observed in 75% of 56 patients with CIN 1 treated and followed for two years after PDT. For CIN 2/3 treatments the sum of the total cure rate after the follow up of 1 and 2 years was observed in 9 patients (90%). Only one patient returned with high-grade lesion.

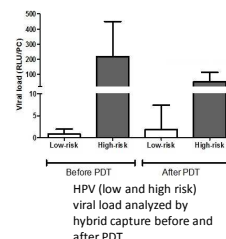


CerCa 150 System®, approved by ANVISA (Brazilian Health Regulatory Agency) and COFEPRIS (Agency in Mexico).



An illustrative image of the clinical procedure.

- ✓ For placebo group (n=14), was observed a complete remission of CIN 1 in 57.14%.
- ✓ The results of hybrid capture are showing a significant decrease (70-80%) in viral load.



CONCLUSIONS

PDT is considered a very attractive technique for the treatment of malignant lesions at an early stage, especially for developing countries.

Another huge multicenter study with over than 250 patients with CIN 2/3 is ongoing, showing that topical MAL-PDT has decreased over than 76% the high-risk HPV load, leading us to conclude that it is a promising technique which may be indicated since the onset of low-grade lesions, and even more, in cases of more extensive lesions.

Acknowledgments:
 The authors thank FAPESP (CEPID/CEPOF 13/07276-1), CNPq and MCTI/FINEP/MS/SCTIE/DECIT (01.130430.00/2013).



Article under review
 by "Pharmaceuticals"



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17th International Photodynamic Association World Congress, edited by Tayyaba Hasan, Proc. of SPIE
 Vol. 11070, 110706Z · © 2019 SPIE · CCC code: 0277-786X/19/\$21 · doi: 10.1117/12.2524706