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File: ■ Turmeric (*Curcuma longa*)
■ Curcumin
■ Human Papillomavirus

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RE: Study of Human Papillomavirus Infection of the Cervix Compares Local Treatments with Curcumin Formula Cream and Curcumin Alone

Basu P, Dutta S, Begum R, et al. Clearance of cervical human papillomavirus infection by topical application of curcumin and curcumin containing polyherbal cream: A phase II randomized controlled study. *Asian Pac J Cancer Prev*. 2013;14(10):5753-5759.

Human papillomavirus (HPV), a common infection, is considered to be the underlying cause of most cervical cancers, especially HPV 16 and HPV 18. Curcumin, a compound found in turmeric (*Curcuma longa*) root, has been reported in preclinical studies to kill cervical cancer cells. Additionally, amla (*Phyllanthus emblica* syn. *Emblica officinalis*) and aloe (*Aloe vera*) in very low concentrations have been found to inhibit transduction of a form of HPV.[1] This randomized, double-blind, placebo-controlled trial investigated a cream product known as Basant™, designed by the Talwar Research Foundation; New Delhi, India. Basant contains curcumin, amla extract, Chinese soapberry (reetha; *Sapindus mukorossi*), aloe, and French rose (*Rosa gallica*) water. Basant was compared with a placebo cream and curcumin and placebo vaginal capsules to investigate the clearing of HPV cervical infections in women who are positive for HPV but free from cancer.

Included women were between 30-60 years old, had diagnosed cervical HPV, with no evidence of cancer or high-grade squamous intraepithelial lesions (HSIL, a form of pre-cancerous pathology), and agreed to use "barrier" contraception during the study. Those with low-grade squamous intraepithelial lesions (LSIL, mild pathology) were included. Those pregnant or lactating or who had more than a 7-day menstrual period, had undergone previous treatment for cervical cancer, or had any serious illness that could interfere with the study were also excluded. In total, 280 patients were intended for randomization into Basant, placebo cream, curcumin capsules, or placebo capsules groups (n=70 per group). However, only 54 patients were enrolled in the placebo cream group as the placebo cream was in short supply from the manufacturer. Neither the content nor the manufacturers of the placebo or curcumin capsules are described.

Patients were screened and randomly assigned in 14 days, with leftover material used to gauge compliance. Treatments were applied once per day for 30 days except during

menstruation. Exact times and amount of clinical visits and follow-up are not well described. At baseline and at the end of the study, Pap smears and cervical samples for HPV detection were collected, colposcopy (microscopic exam) was conducted, and biopsy was done if problems were seen at screening or colposcopy. Polymerase chain reaction (PCR) was used to characterize HPV. Functional assessments of liver and kidneys and hematology were also completed. Adverse events (AEs) were measured and scaled according to mild, moderate, or severe, along with correlation to treatments. All patients enrolled were analyzed for AEs.

In total, 287 women were enrolled in the study, with a significantly greater amount of postmenopausal patients in the placebo cream group as compared to the Basant group (P=0.02). From the total amount of patients, 255 finished the protocol (per-protocol analysis). Those that dropped out due to ASEs but completed the third clinic visit (7 in the Basant group, 3 in the placebo cream group, 2 in the curcumin group, and 1 in the placebo capsule group) were included in the Modified Intention To Treat (MITT) analysis, along with 1 patient that did not complete the full dosage (66 patients in the Basant group, 48 patients in the placebo cream group, 75 patients in the curcumin group, and 80 in the placebo capsule group).

According to the MITT analysis, HPV was cleared in 87.7% of those using Basant cream, in comparison to clearance in 75.0% of those in the placebo cream group; the difference between the 2 groups was notable, but not statistically significant (P=0.08). In the curcumin capsule group, the number of patients (81.3%) who had clearance of HPV was not significantly higher compared to 72.5% of those in the placebo capsule group (P=0.19). When the Basant group results were compared to the combined placebo groups, the difference was significant (P=0.03), but this approach defies the principle of randomized controlled trials.

There were no significant differences in rates of clearance between the Basant cream and curcumin capsule treatment and their respective placebos in the MITT population. Those using Basant cream all (17/17) showed eradication of both HPV 16 and HPV 18 infections, while 85.7% (12/14) of those in the curcumin group cleared the infection; 78.6% (22/28) of those in both placebo groups combined showed eliminated infection. In the Basant group, 57.1% of those with LSIL (4/7 patients) had decreased lesions, while the 2 patients with LSIL in the placebo cream group had no lesions at the end of the study. Two of the 6 patients with LSIL in the curcumin capsule group showed clearance of these lesions, while no one in the placebo capsule group had these lesions at the start of the study.

In the Basant group, 20 patients had AEs, in comparison to 4 patients in the placebo cream group. This difference was significant (P=0.005). Vulvo-vaginal burning was the most common AE in the Basant group (n=12), followed by vulvo-vaginal pruritus (itching; n=10). However, there were no significant differences in the number of AEs reported in the curcumin group compared to the placebo capsule group (12 versus 9 AEs).

Although there was a greater rate of HPV elimination in the Basant group for HPV 16 and HPV 18 as compared to the placebo group (which was not significant [P=0.07]), this product may be clinically useful in treating HPV and preventing cancer. It is suggested that synergy among the botanicals used may enhance bioactivity. Despite this, Basant treatment resulted in significantly more AEs than the placebo group, suggesting that this product may not be well tolerated. Other limitations discussed include the small sample

size in the placebo cream group, combined analysis of the 2 placebo groups, and small number (and inclusion) of patients with LSIL. Additionally, the lack of a comparison of standard pharmaceuticals used to treat HPV to Basant or curcumin treatment is not explained. Also, no rationale is provided for the curcumin formulation employed. Ideally, larger future trials with longer follow up will further address efficacy and tolerability of Basant for HPV clearance.

—Amy C. Keller, PhD

Reference

[1]Talwar GP, Dar SA, Rai MK, et al. A novel polyherbal microbicide with inhibitory effect on bacterial, fungal and viral genital pathogens. *Int J Antimicrob Agents*. 2008;32(2):180-185.

Referenced article can be found at http://www.apocpcontrol.org/page/apjcp_issues_view.php?sid=Entrez:PubMed&id=pmid:24289574&key=2013.14.10.5753.

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