Correspondence

Use of cold atmospheric pressure plasma to treat warts: a potential therapeutic option

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Treating warts can be frustrating for patients and dermatologists alike, as they can recur frequently and often need multiple treatments, which carry a risk of adverse effects. Cold atmospheric-pressure plasma (CAP) is an ionized gas that has been extensively studied for medical applications, including clinical trials for skin conditions. Safety of CAP use on skin has been well demonstrated in the past.[1]

Patient 1 was a 33-year-old man, who presented with four warts on his fingers. The warts failed to improve with over-the-counter products and liquid nitrogen treatments performed over 6 months.

Patient 2 was a 28-year-old man, who presented with a wart on his wrist. He refused cryotherapy because of possible hypopigmentation and he could not afford topical medications.

Both patients were enrolled in a study approved by the Western Institutional Review Board (protocol number: 20130084 and registered on ClinicalTrials.gov (registration number: NCT02759900).

Our CAP source was a pulse generator (FPG10–01NM10; FID GmbH, Burbach, Germany) supplying 20 kV pulse of 20 ns pulse width at 400 Hz to a quartz-covered copper electrode (10 cm in length, 1 mm thick quartz cover, 5 mm total diameter (Fig. 1). Duration of treatment was 2 min/lesion.

The thickest (right thumb) lesion of Patient 1 cleared after two treatment, and the other lesions after three treatments (Fig. 2), and remained clear 7 and 6 months later, respectively. Four months after the start of treatment, a new wart appeared on the left thumb, which cleared with three treatments.

Patient 2 was treated twice and, according to him but not confirmed by us, the wart improved but never resolved. He never returned for subsequent treatments. By the time of his 5-month evaluation, the wart had recurred (Fig. 2).

We treated two patients with a total of six warts. Our first patient had resolution of all lesions; he later developed a new wart during the observation period, which also cleared after three treatments. This suggests that our results were due to a local CAP effect and not a generalized immune response.



Figure 1 Device used for wart treatment. Custom-built cold atmospheric pressure plasma device with handheld electrode.

The second patient reported improvement of his single lesion, but it recurred after treatment was stopped, indicating that CAP did not have a lasting inhibitory effect on the partially cleared wart. It is unknown if continuing treatments would have altered the outcome.

We are not aware of previous *in vivo* or *in vitro* models to explain the effect of CAP on warts, but CAP has been shown to selectively induce apoptosis in malignant cells *in vitro*.[2] *In vivo* efficacy of CAP in treating actinic keratosis has also been reported.[3,4] It can be hypothesized that CAP may induce apoptosis in warts. It has been reported that CAP inhibits adenoviruses,[5] possibly by altering the virus capsid. It is feasible that the capsid of human papilloma virus, a similarly nonenveloped DNA virus, is also susceptible to CAP-induced damage. Although the mechanism of action is unclear, and the number of treated lesions was very small, meaning that larger follow-up studies are needed, the results of this proof-of-concept study are promising, with clinical improvement of warts achieved by CAP treatment and lack of recurrence of fully cleared lesions after several months. Encouragingly, the cost of a market-ready CAP device could be on par with current electrosurgery tools.

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Figure 2 Treatment of warts with cold atmospheric pressure plasma. (a–e) Patient 1. (a,b) Partially subungual wart located on the thumb tip (a) before the first treatment and (b) 5 months after the second treatment; (c–e) wart on index finger (c) before treatment, (d) 2 months after the first treatment and (e) 4 months after the third treatment (the other two treated lesions of this patient are not shown.) (f,g) Patient 2. Wart on the wrist (f) before treatment and (g) 5 months after the second treatment (the patient was unavailable for additional treatments or interval evaluations).

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