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COMPARATIVE STUDY OF 5% POTASSIUM HYDROXIDE SOLUTION VS. 0.1% TRETINOIN LOTION IN THE TREATMENT OF PLANE WARTS: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background and Objective: Plane warts are considered a common therapeutic problem. An extensive armamentarium of physical, chemical, surgical, and immunological therapies have been employed, but none of them proved to be uniformly efficient. We sought to compare the efficacy and safety of potassium hydroxide (KOH) solution vs. tretinoin lotion in the treatment of plane warts.

Materials and Methods: A total of 72 patients participated in a 6 week trial. They were randomly assigned to receive either 5% KOH solution (KOH group) or 0.1% tretinoin lotion (tretinoin group). The patients were assessed at the 2nd, 4th, and 6th week after the treatment period for the cure rates and clinical complications. Also, the patients were followed up for two weeks to detect any recurrence.

Results: After 2, 4, and 6 weeks of treatment period in both groups, the mean number of lesions decreased. Reduction of lesions at the end of study was 59.8 % and 64.1% in KOH and tretinoin groups, respectively but no significant difference were observed between two groups (P= 0.39). There was no relapse of lesion after two weeks follow- up period.

Conclusion: Potassium hydroxide solution was found to be effective similar to 0.1% tretinoin lotion in the treatment of plane warts. In the KOH group adverse effects was relatively more than tretinoin group but, it was clinically negligible.

Keywords:

Plane wart, Potassium hydroxide (KOH), Therapeutics, Tretinoin

Introduction

Warts result from a hyperkeratotic reaction to human papillomavirus (HPV) infection (1-5). Plane warts as the common dermatological disease usually affect the face and the dorsa of the hands (6, 7). Although no viral subtype is absolute in the development of plane warts, the infection is typically associated with HPV types 3, 10, 28, and 41 (8-12). Plane warts are a frequent therapeutic problem; however, they regress spontaneously through the cell-mediated and humoral immunity (6-9, 13). A wide armamentarium of surgical, physical, chemical, and immunological therapies have been used but none of them proved to be uniformly efficient (1, 6, 14-16). Different types of warts may need different site-dependent treatments and therapy does not affect transmissibility (16).

Topical 0.05% tretinoin has been used for the treatment of plane warts (17). There is some evidence that retinoids can down regulate HPV transcription in affected cells. In addition, retinoids disrupt epidermal growth and differentiation and are considered a potent strong immunomodulator (16).

Potassium hydroxide (KOH) is a potent alkali (18) with well-known keratolytic properties and dermatological uses in the treatment of male genital wart and *Molluscum contagiosum* (19-22).

Potassium hydroxide digests proteins, lipids, and most other epithelial debris of skin scrapings to identify fungal infections of skin, hair and nail. It also, destroys keratin and penetrates deeply into the skin (22-26).

In the medical literatures a few studies have evaluated the efficacy of KOH in the treatment of plane warts (4). Therefore, we undertook a 6-week period study to test the efficacy and safety KOH 5% solution vs. 0.1% tretinoin lotion in patients with plane warts.

Materials and Methods

Study Design and Population

We conducted a randomized controlled trial to attain a therapeutic modality for the plane warts at a teaching hospital in Ahvaz- Southwest Iran from March 2010 to March 2011. A total of 72 patients with at least three plane warts established by dermatologists were included the study. In doubtful cases, a biopsy and histopathological examination were made. Exclusion criteria were the patients who had received any medication in the past four weeks, secondary infection, pregnancy, and breastfeeding. The patients were randomized to receive either 5% KOH aqueous solution (34 patients) or 0.1% tretinoin lotion (38 patients). Ethical Committee of Ahvaz Jundishapur University of Medical Sciences approved the study. Furthermore, this trial was carried out in accordance with the Declaration of Helsinki and subsequent revisions. The patients were counseled before the study and signed the informed consent form.

Treatment Protocol

An aqueous solution of 5% KOH was prepared by dissolving 5 g of powdered potassium hydroxide (Merck, Germany) in 100 ml of distilled water and the patients received it free of charge. On the other hand, the patients were referred to a particular pharmacy to prepare 0.1% tretinoin lotion (Sutur Paris, France). A resident of dermatology applied the KOH solution by cotton tipped stick at the first visit. Then the patients or their parents were taught how to use the medication at night and to washing in the morning.

In addition, in the tretinoin group, the patients were instructed in the use of 0.1% tretinoin lotion. At each visit, the number of lesions was recorded and the patients were queried regarding adverse events using a checklist by a resident of dermatology. At the end of sixth weeks of treatment, the patients were followed up for a 2-week period. Data analysis was performed using SPSS 11.5 and results are presented as Mean \pm SD. We used analytic statistics t-test, and multivariate logistic regression. Also $P < 0.05$ was considered significant.

Results

There was no significant difference between the groups according to the basic demographic data (Table 1).

Table-1: Demographic characteristics of study population.

	KOH Group	Tretinoin Group	<i>P</i>
Age (mean \pm SD)	15.3 \pm 10.238	17.1 \pm 10.38	0.46
Gender	26 (68.4) F 12 (31.6)M	23 (67.6) F 11 (23.4) M	0.89

We did not find any statistically significant difference in the duration of the lesions in KOH (17.3 \pm 10 months) and tretinoin (17.2 \pm 7.7 months) groups ($P = 0.85$). One patient in tretinoin group was dropped out the study after 4 weeks of trial because the lack of treatment satisfaction. After 2, 4, and 6 weeks of treatment period in both groups, the mean number of lesions decreased. Reduction of the lesions at the end of the study was 59.8 % and 64.1% in KOH and tretinoin groups, respectively. There was no significant difference in reduction of the lesions between the groups ($P = 0.39$) (Fig. 1). Also, we did not find any relapse in the groups after 2 weeks follow-up period (Fig. 2).

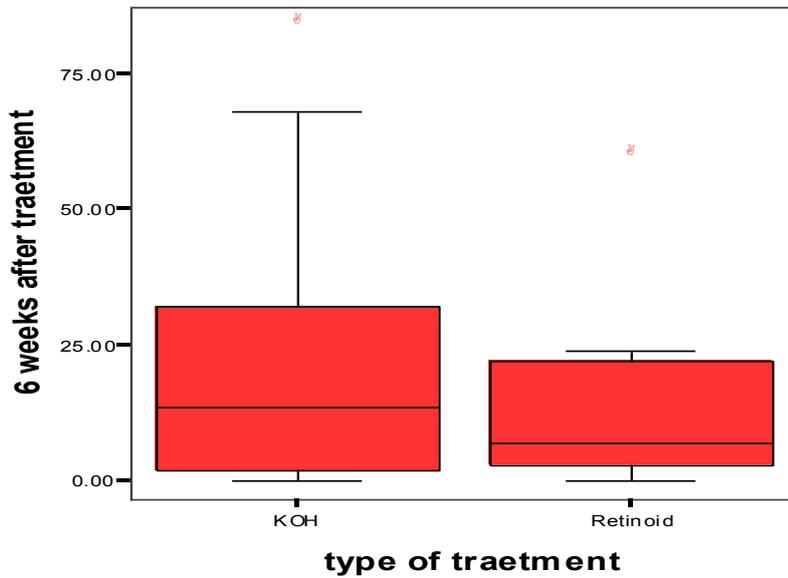


Fig. 1. Comparison of the lesions after 6 weeks treatment in KOH and retinoid groups.

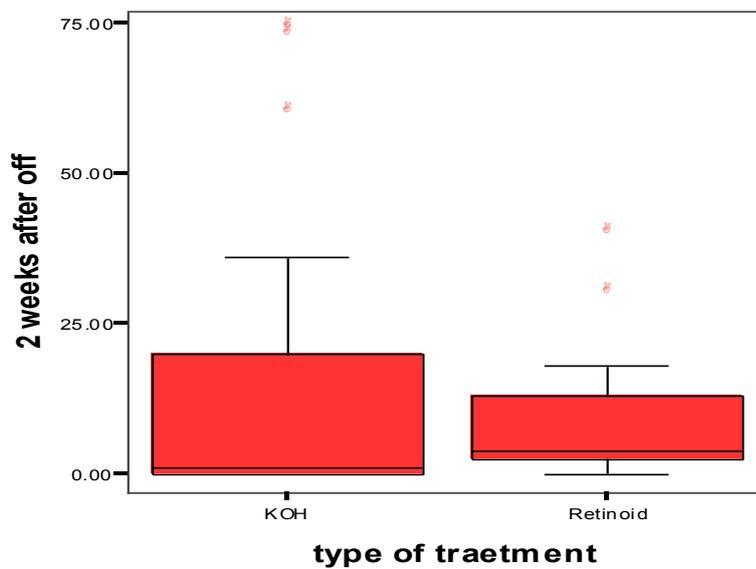


Fig. 2. Comparison of the lesions after 2 weeks follows-up in KOH and retinoid groups.

There was not a significant correlation in the number of decreased lesions between the groups ($P > 0.05$). Additionally, multivariate logistic regression analysis revealed that the decrease of lesions was not related to the gender, age, and previous treatment.

Clinical Complications

All adverse events were recorded at each visit. The side effects included erythema, scaling, crust, dyspigmentation (hypo- or hyperpigmentation), secondary infection and burning sensation. A significant difference was indicated in the rate of adverse effects in the two groups (Table 2).

Table 2: Complications in KOH and Tretinoin groups.

Complications	KOH Group	Tretinoin Group	<i>P</i>
Erythema (%)	11 (29.6%)	13 (38.2%)	0.49
Scaling	5 (14.7%)	3 (8.8%)	0.001
Crust	13 (34.2%)	0(0%)	0.001
Secondary infection	1 (2.6%)	0(0%)	0.41
Hyperpigmentation	4 (10.5%)	5 (14.7%)	0.68
Hypopigmentation	1 (2.6%)	0 (0%)	0.38
Burning	17 (44.7%)	5 (14.7%)	0.001

Discussion

Many therapeutics options are available for HPV-induced lesions (41-44). The present trial evaluated the role of topical KOH as a novel agent in the plane warts management. In this randomized study 5% KOH aqueous solution was found to be effective similar to 0.1% tretinoin lotion in the treatment of plane warts. According to the current research both prescribed medications were able to reduce the facial plane warts, but the difference was not considerable between the two groups. Also, no correlation was observed between the age and gender with response to the treatment in the both groups. That means KOH and tretinoin can be applied in both gender and in all age groups. Also, the present study indicated that the previous treatments do not affect response to tretinoin and KOH therapy. We did not find any association between the locations of the lesions with response to the treatment. In our investigation, KOH clinical complication was higher than tretinoin therapy; however, KOH therapy was not painful and scarring. There was an association between the duration of warts and therapeutic response in which lesions with longer duration demonstrated more response to the treatment. There are plausible mechanisms for the efficacy of KOH in the plane wart treatment. It is supposed that KOH act as a keratolytic agent and also induce inflammatory response; therefore, it leads to the destruction of the virus-infected cells.

Notably, several medical literatures have confirmed the role of KOH in the management of warts. Al-Hamdi and Al-Rahmani evaluated the efficacy and tolerability of KOH solution in the treatment of plane warts. They demonstrated that topical KOH might be an effective and safe therapy in concentrations 5% and 10% with no considerable adverse effects. Loureiro et al. (18) investigated the therapeutic role of 5% KOH aqueous solution in 35 male patients with genital warts. This study indicated over 85% of complete clearance of the lesions with 9% recurrences rate after the follow-up period.

Most patients had local reaction, varying from erythema to minor erosions. Our study compared with the study of Loureiro et al. showed the less complete clearance. It may explainable with the location of the lesions because the moisture and PH of the genital skin can make a difference in the outcome of the treatment. According to the present study, the highest response was seen at the first two weeks while the lowest response were at the fourth and sixth week.

Notably, clinical response directly was associated to the number of primary lesions. In the other words, the patients with more initial lesions were more sensitive to the both medications. In our trial adverse event of scaling in retinoid group was higher while, crust and burning sensation in the KOH group was more prominent. In the study of Kubeyinje (17) retinoid complications such as redness and peeling was 42% that it was similar to our study. In contrast, the clinical complications of KOH therapy were less observed in the studies of Loureiro (18), Romiti (26), and Mahajan (45).

The limitations of the present research were the small number of patients and short follow up period. We suggest performing future studies with larger sample size and more prolong follow up duration. Additionally, the application of other concentrations of KOH solution (10% and 15%) with placebo control group is recommended. The KOH solution also may be suggested in combination therapy with the current modalities for the plane warts management.

Conclusion

Our finding demonstrated that 5% KOH aqueous solution was effective similar to 0.1% tretinoin lotion in the treatment of plane warts. In the KOH group adverse events was relatively more than tretinoin group but, it was clinically negligible.

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