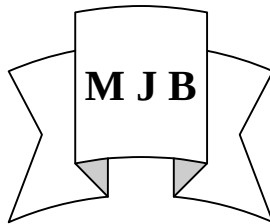


Evaluation of The Efficacy of Contractubex Gel in Plane Wart Treatment

Kareema Amine Al-Khafaji

Babylon University, College of Medicine



Abstract

Treatment of plane warts is a problematic. Methods such as a combination of salicylic acid with lactic acid lotion, cryotherapy and cauterization are used but they are associated with high recurrence rate, risk of scar, pain and high cost. In addition, treatment with topical tretinoin lotion causes an irritant contact dermatitis that limited its use. Contractubex gel consists of heparin sodium 5000 I.U, extre cepa 10g, allantoin 1.0g in water-soluble, fat free gel, exerts a softening and smoothing effect on indurated, hypertrophic, painful and cosmetically disfiguring scar tissue. In this study, the efficacy of contractubex gel in treatment of plane warts was evaluated and compared with 0.05% tretinoin lotion treatment. The results, after six weeks follow up revealed that up to 79.4% of the lesions in contractubex gel treated group diapered versus 20.6% of the lesions in tretinoin treated group. This modality of treatment seems to be superior to tretinoin lotion in the treatment of plane warts and even the common type, which is due to high efficacy of contractubex gel associated with low incidence of side effects. This is the first use for this drug in the treatment of viral warts.

الخلاصة

يعد علاج التاليل المسطحة مشكلة علاجية يعالج بمحلول خليط لاسيك اسد والاكتك اسد بالتجميد والكي ولكن هذه العلاجات مصحوبة بنسبة عالية بروجوع المرض ، تخلف ندب ،الم مع تكاليف السعر بالاضافة للمعالجة بمحلول الترتينوين بسبب اكزيما تماسية مما يحدد استعماله يحتوي الكونترنترانتوبكس جيل على صوديوم الهيبارين 5000 وحدة مستخلص البصل 10 غرام الانتوين 1 غم ، والمثليفة والتاركة انسجة مشوهة جماليا . في هذه الدراسة تم اختبار تأثير الكونتر انتوبكس جيل في علاج التاليل المسطحة مع مقارنة ذلك مع المعالجة بمحلول الترتينوين 0.05% النتائج بعد المتابعة لمدة ستة اسابيع وجدت ان 79.7% من التاليل التي عولجت بعقار الكونترانتوبكس جيل قد اختفت مقارنة بال 20.6% بمحلول الترتينوين 0.05% هذا النوع من العلاج يعد فائق في تأثيره في علاج التاليل المسطحة وحتى الشائعة لما له من تأثير كبير وسريع وبمضاعفات ضئيلة وهذه اول مرة تم فيها استعمال هذا العقار لمعالجة التاليل .

Introduction

Warts are benign proliferations of the skin and mucosa that result from infection with human papilloma virus. Plane warts are smooth flat-topped papules most commonly found on the face, back of the hands and lower legs associated usually with skin colored or light brown coloration. They become inflamed as a result of an immunological reaction just before they resolve spontaneously (1, 2).

A variety of therapeutic modalities with different mode of action are available such as a combination of salicylic acid and lactic acid, trichloracetic acid, silver nitrate, potassium hydroxide, fluorouracil, interferon, retinoid, cimetidine, 5-aminolacvalinic acid, cryotherapy, Laser therapy electro-cauterization and surgical excision (3, 4, 5). Mostly these modalities of treatment are associated with pain, inconvenience, risk of scarring and hypo or hyper pigmentation especially on the face. Cosmetic and psychosocial problems might be ended with some of these modalities of treatments (2). Retinoic acid may be applied topically in plane warts, although the best results are claimed for higher than usual concentration and associated with irritations as a common side effect (5).

Contractubex exerts a softening and smoothing effects on indurated hypertrophic, painful, and cosmetically disfiguring scar

tissue. The water soluble gel base mediates the deep penetration of the active ingredient into the skin, there by affording an intensive local

try to use it in the treatment of plane warts. To our knowledge, this is the first time that contractubex gel is used in the treatment of plane warts in comparison to 0.05% tretinoin lotion treatment.

Material and methods

During the period 2005-2007, seventy-five consecutive patients were examined in a private clinic as well as an out-patient clinic of the dermatological department in Mirjan-teaching hospital/Hilla. The diagnosis of plane warts was achieved. The patients involved in this study were chosen to have two sided body located plan warts and they were included in this double blind self-control comparison.

Patients with systemic diseases such as diabetes mellitus, asthma, renal insufficiency, patients who were consuming immunosuppressive drugs (e.g. renal transplants..etc), pregnant and nursing women were excluded from this study. All patients were received full information on the purpose and design of this study. They were informed do not received any systemic or topical wart treatment within four weeks

before entering the study. Detailed history sheet for every patient admitted to the study

was taken including number of the lesions in each area of the body as well as age, sex and address.

For each patient, lesions of one side of the body were treated by the application of contractubex gel and the other side by 0.05% tretinoin lotion (twice daily with each treatment). Solutions were applied on the lesions by a wood end of a cotton swab to minimize filtration of effective drug to the surrounding areas. For the children who were aged less than ten years, their parents were asked to apply the treatments. The side that was treated by intermittently selected for each patient should be fixed and registered in checklist.

Contractubex is a trade mark for an onion extract-containing gel preparation manufactured by Merz pharm GmbH&co.KGaA 60318 Frankhurl am Main, Germany, and designated for topical treatment of cicatrices (such as disfiguring scar tissue, contracture, etc). The preparation contain 10% *Bulbus allii cepae* extract, heparin sodium 5000 IU, allantoin 1g, and methyl-4-hydroxybenzoate 150 mg. The ether extract contain oils of *allium cepae* (0.005-0.15%), cyclo-alin-methyl-alein, propylalin, thiopropional-camphophelol, quartz derivatives, phloroglucin peptides, protocatechin acid, ferulic acid, amino acids,

pectin phytohormones, vitamin C up to 33 mg, and vitamin B1 up to 60 mg. The gel is supplied in tubes of 20, 50, and 100g.

Duration of the treatment was planned to be six weeks and a control visits were arranged every three weeks intervals. The number of warts in the examined side of the body and any adverse effects related to the study preparation such as burning sensation, pruritus, erythema and contact dermatitis were recorded in each visit. Evaluation of the efficacy of the treatment was based on reduction of the number of warts. Statistical analysis was performed by the Chi-square test and value of $P < 0.01$ was considered significant.

Results

75 patients were participated in the entire study. Out of 75 patients 54 (72%) were females and 21 (28%) were males. The distribution of patients in different age groups was shown in (table 1). The peak incidence of plane warts was (30.7%) ranged between the age group 1-10 years . The over all number of the lesions were (1482); 752 lesions were treated by application of contractubex gel and 730 lesions were treated by 0.05% tretinoin lotion. In the first three weeks of treatment with contractubex gel 275 lesions (1st treats), and with 0.05% tretinoin lotion 65

lesions (2nd treats) were disappeared , In the second three weeks of follow up another 355 lesions in the first treats and 98 lesions in the second treats were disappeared , The total number of plane warts were 630 (79.4%)warts disappeared by contractubex gel versus the disappearance of 163 (20.6%)with 0.05% tretinoin lotion (table 2). The clinical significance of contractubex gel was (79.4%) and 0.05% tretinoin lotion (20.6%) was high, P.value is< 0.001. Regarding the time of improvement for each treatments have significant difference with time P.value is<0.001.So both treatments have significant difference with 3weeks, 6weeks P.value is <0.001. there is no significant side effects apart of mild dryness of skin. This treatment is also effective and can be used for common warts, milia, and syringoma.

Discussion

Warts are benign, often spontaneously resolving, epidermal proliferations. Plane warts (juvenile) are caused by human papiloma virus (most often HPV-3 and HPV-10) and generally multiple, slightly elevated, smooth papules occurring most often on the face, hands, neck and legs of children and young adults (5,6). They may be in a group and linear arrangement

implying a role of trauma (Koebner phenomenon) . The nature of warts is unpredictable. They often fail to disappear with treatment or they recur after apparent cure. Some warts resolve spontaneously and thus the evaluation of treatment may be difficult. There is no way to prevent warts and both patients and physicians often become frustrated by an apparent endless appearance of new warts.systemic medications are not successful and locally destructive methods are the mainstay of therapy.

The aim of treatment is to destroy the wart and to spare the normal skin with out causing distress to the patient or scarring as well as with minimal pain and inconvenience (7,8,9, 10,11).

Many researchers have studied about plane wart treatment. In a randomized controlled study of 25 children, 85% of warts disappeared with 0.05% tretinoin cream compared with 32% in controls.⁽⁶⁾ In this study, efficacy of tretinoin was less (53.7%) than contractubex gel. Retinoid are involved in the regulation of diverse biologic functions. They affect cell growth and differentiation, morphogenesis ,tumor promotion and malignant cell growth, also exert immunomodulatory action and alter cellular adhesiveness(12)

Molluscum contagiosum, warts and various forms of ichthyosis may be improved by topical retinoids to a variable degree (12). It has been well-documented that Tretinoin (all-trans retinoic acid) increases proliferation of basal keratinocytes and also the number of cell layers expressing the differentiation markers involucrine, loricrine, fillagrin and epidermal transglutaminase (13). These epidermal changes collectively translate to clinical desquamation and peeling and mediated by nuclear receptors of retinoids(13). Induction of desquamation and immunomodulation may be the probable mechanism that explains the efficacy of tretinoin in plane wart treatment. In a randomized controlled study of 25 children, 85% of warts cleared with 0.05% tretinoin cream compared with 32% in controls(6), in other study the result was less(53.7%)(7), while in our study the result was lesser(20.6%).

The mechanism of action of contractubex gel in treatment of plane warts is proposed to be;

- 1-the active ingredients of contractubex gel has ability of penetration into the plane warts causing softening and inflammation of the lesions after which resolution and disappearance of the lesions and spare normal skin.

- 2-presence of vitamin C and vitamin B1 that proved to be effective in treatment of viral warts. Vitamin C is a powerful antioxidant that fights destructive, unstable molecules called free radicals. It strengthens cell walls in body tissues and boosts immunity, which helps the body fight viruses. It can be helpful against warts both as an oral supplement and as a topical treatment. And vitamin B Important in normal cell multiplication(12, 13, 14, 15).

Conclusion :Contractubex gel appears as an effective, safe and cost-effective treatment in plane wart.

References

- 1-Hunter J.A.A., Savin J.A and Dahi M.V. Infectious diseases in clinical Dermatology, 3rd. edition, Black w Science, 2002; p201.
- 2-Lowy DR, and Androphy EJ. Warts. *In: Freedbe IM, Eison AZ, et al Fitzpatrick's Dermatology in General Medicine*, 6Th ed. McGraw- Hill Co: New York; 2004. P. 2119-2129.
- 3-Benton EC. Human papillomavirus infection and molluscum Contagiosum. *In: Harper J, Orange A, Prose N. Textbook of Pediatric dermatology*, 1st ed. Blackwell Science: Oxford; 2000. p. 313-6.
- 4-Sterling JC: Virus infections. *In: Burns Breathnach S, Cox N, Griffith's C, et al. In: Roo textbook of dermatology*, 7Th ed. Blackwell Science UK; 2004. p. 25-50.

- 5-Kubeyinje EP. Evaluation of the efficacy and safety of 0.05% tretinoin cream in the treatment of the plane warts in Arab children. J Dermatol Treat 1996; 7:21-2.
- 6-Anahita Vali,N and Fedowski, F. *Ferdowsi*. Acta Dermatol Venereol 2000;80:134-135.
- 7-Jacyk WK, de Villers EM. Epidermodysplasia verruciformis and health effects in humans. Am J Clin Nutr. 1999; 69(6):1086-1107.
- 8-Van Wyk, CW, Focal epithelial hyperplasia of the lip recently discovered in South Africa. Brit J Dermatol 1977;96:381-388.
- 9-Sparling JD,Checketts SR, Chapman MS. Imiquimod for planter and periungual warts. Cutis 2002; 68:397-399.
- 10-Grussendorf-Conen EI, Jacobs, Rubben A,et al. Topical 5% imiquimod long-term treatment of cutaneous warts resistant to standerd therapy modalities. Dermatologyu 2002;205:139-145.
- 11-Culter K. Kagen MH, Don PC et al.Treatment of facial verrucae with topical imiguimod cream in a patient with Human Immunodeficiency Virus. Acta Dermatol Venereol 2000;80:134-135.
- 12-Carr AC, Frei B. Toward a new recommended dietary allowance for vitamin C based on anti-infective and health effects in humans. Am J Clin Nutr. 1999; 69(6):1086-1107.
- 13-Johnston CS. Recommendations for vitamin C intake. JAMA 1999;282(22):2118-2119.
- 14-American Academy Of Dermatology 930N. Mecham Road ,P.O. Box 4014.Schamburg IL.60168- 4014.(847)330-0230.Fax(847)330-0050.
- 15- American Academy Of Family Physicians .8880 Ward Parkway.Kansas City, M

Table (1) Distribution of the patients in different age groups

Age group (years)	Number of patients	Percentage
1-10	23	30.7
11-20	17	22.7

21-30	16	21.3
31-40	13	17.3
41-50	6	8.0

Table (2)The number of warts before and after treatment

The type of drug	Number of warts before treatment	percentage	Number of warts disappeared after three weeks of treatment	percentage	Number of warts disappeared after six weeks of treatment	percentage	Total number	percentage
Contractubex gel	752	100	275	43.7	355	65.3	630	79.4
0.05% tretinoin lotion	730	100	65	35.5	98	64.5	163	20.6
summation	1482		340		453		793	100