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Case Report Open Access

Successful Treatment of Plantar Warts with Bleomycin using Multi-Puncture Technique and review of Multi-Puncture Applications

Temel AB[1]* and Akman-Karakas A[2]

[1]Faculty of Medicine, Akdeniz University, Antalya, Turkey
[2]Akdeniz University, Antalya, Turkey

Backround/Introduction

Warts are rough, scaly, spiny papules or nodules. They can be exist on any cutaneus surface and they are a manifestation of human papillomavirus (HPV) infection. There is no treatment, which is 100% effective and different types of treatment can be utilised. 16% Salicylic acid is the best option which is suggested due to evidence based analysis and for second line treatment cryotherapy is suggested. Bleomycin is considered as third line therapy, especially encouraged for resistant warts to conventional methods. According to the modified evidence based medicine system, bleomycin has been regarded as level 1 strength of evidence for the treatment of warts [1]. Bleomycin is derived from '*Streptomyces verticillus*' and has an antiviral activity by inhibiting DNA synthesis. Since 1970s, numerous reports have been published on the use of intralesional bleomycin for the treatment of warts, with cure rates ranging from 14% to 99% [2]. Another administration procedure of bleomycin is utilising multipuncture technique which is also thought to be safe and effective [3-7]. Very few studies are available about this technique of bleomycin administration in the current literature. There is no concensus about procedure for application, the frequency of application, concentration and dosing schedule. In this presentation, , we report a case which responded to multipuncture administration of bleomycin for her recalcitrant plantar warts and multipuncture technique for warts so far are summarized and compared.

Case report

A 56-year-old woman presented to our clinic with 3-year history of plantar warts. She has been treated with salicylic acid and flourourasil combination for 1 month and cryotherapy (for 5 times with 3-week interval) without any success (Figure 1). Treatment with multipuncture technique of bleomycin was started. No other local and systemic treatment were given. She has no history of any other illness. We used a vial containing 15 Units, 5 mL of normal saline solution was added to have a concentration of 3 U/mL. We have used a povidone-iodine swab before injection. Then we have used a sterile 26 gauge hypodermic needle and randomly pricked the warts. The needle was penetrated to the base of the warts until we sensed resistance. Then occlusion with a sterile gauze which was dropped 1 ml of the prepared solution of bleomycin is applied and kept with stretch film for 12 hours. This procedure was repeated every two weeks for a period of 2 months (four times). Photograph of each lesion was also taken at every visit. After each application plantar warts gradually healed. At the end of 2 months complete resolution is observed (Figure 2). Patient experienced any side-effects beside local pain during pricking. The patient is followed with no sign of recurrence for another 18 months. Informed consent has been obtained.

Discussion

As is seen in our case report, multipuncture technique of bleomycin therapy for warts is a safe, effective and well tolerated treatmet. Bleomycin's efficacy is thought to depend on its effects on cellular DNA, which impede viral survivability by limiting turnover of host cells [8]. Because of it's toxic nature as a chemotherapeutic agent and increased incidence of adverse effects, bleomycin administration has been limited to unresponsive cases. Multipl delivery techniques have been utilised so far and multipuncture applications of bleomycin are summarized and compared in this review (Table 1). The multipuncture technique

Figure 1: Warts before multi-puncture application of bleomycin.

Figure 2: Complete recovery after bleomycin application.

***Corresponding author:** Dr. Aslı Bilgiç Temel, Faculty of Medicine, Akdeniz University, Antalya, Tuekey, Tel: 902422496704; E-mail: taocy@cqu.edu.cn

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Study/ year	Study design	Number of warts	Location of warts	Past treatments/ (%) percentage of cases which used therapies before bleomycin	Method	Range of application	Concentration of bleomycin	Duration of follow-up	Complete clearance	Side effects
Shelley et al. [3]	Nonrandom, Nonblind, prospective clinical trial	258	Palms, soles, dorsal aspect of hands and feet, forearms, face, penis, knees, paronychial areas	Cryotherapy,salicilic acid, surgery/ (40%)	a bifırcated vaccination needle 40 times per 5 mm2 dry derssing for 24 hour	3 weeks/ once	1 U/ml	6 months	92%	Local pain
Munn et al. [4]	Nonrandom, Nonblind, prospective clinical trial	62	Palmar, plantar, periungal	Unsuccesful conventional therapies/ undetermined	Topical lidocain for 1 hour Monolet needle	4 weeks/ 4 times	1 U/ml	12 months	92%	Local pain
Sardana et al. [5]	clinical case report	1	Periungal-subungal	Unsuccesful to topical salicilic acid, electrocoutery, CO2 laser/ undetermined	26 gauge hipodermic needle occlusion for two hours	4 weeks/ 5 times	1U/ml 2 ml	14 months	100%	Local pain, inflamation, eschar formation
Alghamdi et al. [6]	Nonrandom, Nonblind, pilot prospective clinical trial	15	periungal	Unsuccesful topical salicilic acid, electrosurgery, pulsed dye laser/ (80%)	İntralesional lidocain 2% for 1 hour 27 gauge needle Topical antibiotic applied simple dressing	4 weeks / one or two times	0.1 U/ml 1 ml	6 months	86.6%	Local pain, mild hyperpigmentation
Alghamdi et al. [7]	Nonrandom, Nonblind, pilot prospective clinical trial	23	plantar	Unsuccesful topical salicilic acid, electrosurgery, pulsed dye laser/ (34%)	İntralesional lidocain 2% for 1 hour 27 gauge needle Topical antibiotic applied simple dressing	4 weeks/ one or two times	0.1 U/ml 1 ml	6 months	74 %	Local pain
Current case	Clinical case report	3	plantar	Salicilic acid-flourourasil combination, cryotherapy	26 gauge needle Occlusion for 12 hours	2 weeks/ 4 times	3 U/ml 1 ml	18 months	100%	Local pain

Table 1: Multipuncture applications of bleomycin for warts so far are summarized and compared.

first described by Shelley and Shelley [3], has been helpful in treating warts in different localisations. They have used a bifurcated vaccination needle to introduce bleomycin sulfate (1 U/ml) into warts. 92% of a random series of 258 warts have been eliminated after a single treatment in this trial. 9% of patients required two to seven treatments for wart eradication. They haven't observed recurrence during a 6-month follow-up period [3]. In 1996 Munn [4] have used a new technique of bleomycin injection for palmar, plantar and periungal warts. 1 mg/ml bleomycin solution was dropped on to the wart and pricked into the wart using a Monolet needle. They achieved 92% success [4]. In 2010 Sardana [5] used the "prick" method of administering bleomycin for periungal-subungal wart. They have used 1 U/ml concentration of bleomycin. For prick method they used a ring block and randomly pricked the wart with a sterile 26 gauge hypodermic needle. Then they sprayed 2 ml of the prepared solution of bleomycin on to the wart tissue. The modification in their case was the occlusion which is applied for 2 hours. They repeated this procedure once a month for a period of 5 months with complete resolution of the wart. The patient has been followed up with no sign of recurrence for another 6 months [5]. Multipuncture tecnique of bleomycin was found to be effective even at very low concentrations. AlGhamdi [6] have utilised translesional multipuncture treatment with a low concentration (0.1 U/ml) of bleomycin and pricked the periungal warts with a sterile 27 gauge needle. They have achieved 86.6% complete clearance of warts at the 6 month follow-up with only one injection. There was no significant long-term adverse effects [6]. In 2012 AlGhamdi [7] have done a similar study on plantar warts. The results showed 74% complete clearance of warts. Also no significant long-term adverse effects were seen [7]. Decrease in the success rate of this administration may be based on low concentrations of bleomycin or the limited number of applications compared to the other studies. Because when we analysed efficacy of studies, response to therapy was observed to be higher in high bleomycin concentration (Table 1). When we evaluated the other studies for increasing effectiveness of multipuncture technique we choised using high concentration, frequent application and occlusion. The multipuncture technique is developed for avoiding adverse effects of intralesional bleomycin. Truely this technique provides an advantage over other treatment modalities with low occurence of adverse events [7]. Sardana [5] and AlGhamdi [7] both have thought intradermal injection of bleomycin can sometimes be given either too deep or shallow [5,6]. AlGhamdi [7] suggested that multipuncture tecnique provides homogenous distribution of bleomycin throughout the entire wart. This technique reduces localized high concentrations of bleomycin on the wart, controls the depth of injections. Also they suggested that practitioners can avoid introduction of bleomycin into the dermis by this technique [5,6]. Also bleomycin therapy is required less equipment than cryotherapy, it would be more suitable for peripheral practice [9]. İn addition, easy pain management and

shorter pain period is a winning edge of bleomycin [10] especially by multipuncture technique. In the current case we used 1 ml of 3 U/ml concentration of bleomycin. Even if we used high concentration, frequent application and occlusion we haven't noted any adverse effects except pain during pricking. So we thought that we provided increase effect on warts. In the following years multipuncture bleomycin therapy can be more top spot in the treatment algoritm of recalcitrant warts owing to fewer side effects, fewer systemic effects, well efficacy, easiness of application features instead of intralesional blemycin. Further studies are required for specifying the standard dose and method of administration in multipuncture tecnique to determine the location of this method in the treatment of warts.

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