ORIGINAL ARTICLE

Efficacy of botulinum toxin type-A (BT-A) in multiple eccrine hydrocystomas

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ABSTRACT

Background: Although many treatments have been suggested for eccrine hydrocyctoma so far, most of them are disappointing. The autonomic inhibitory effect of botulinum toxin type-A (BT-A) can result in successful treatment of eccrine hydrocyctoma.

Objective: This study was performed to evaluate the efficacy of BT-A in treatment of eccrine hydrocyctoma.

Methods: Twenty two patients (16 females and 6 males) with eccrine hydrocyctoma documented pathologically were divided into two groups. In the first group (12 patients) and second group (10 patients) BT-A (dysport) was injected perilesional intradermally at a concentration of 5 and 10 units in 0.01 ml respectively.

Results: Mean time duration of drug efficacy was 7.3 and 6.9 months in the first and second groups respectively (p value=0.840). Nine patients (75%) in the first group and 8 patients (80%) in the second group showed excellent response at first session treatment respectively (p value=0.727). Transient asymmetric smile was observed in two patients in each group.

Conclusion: BT-A which is injected intradermally at very low dose is a safe and rapid treatment for eccrine hydrocyctoma. Even though complications are mild and transient but necessity of repeated treatment are major limitations of this drug.

KEYWORDS: Eccrine hydrocyctoma, botulinum toxin type-A, dysport, autonomic inhibitory effect

INTRODUCTION

Eccrine hydrocyctoma (EH) is a rare benign tumor that consists of mature and deformed eccrine sweat units with ductal cystic dilatation that mostly involves middle-aged women.[1]

EH may be either solitary (Smith type) or multiple (Robinson type) that clinically presents as uniform dome-shape, skin colored or translucent papules and nodules with bluish hue usually suited on periorbital region.[2] The lesions are more prominent during hyperhidrosis, in warm climate, during physical exercise, sun exposure and in graves' disease.[3, 4]

Clinical characteristics of EH are very similar to apocrine hydrocyctoma. Nonetheless, multiplicity, periorbital location and seasonal and temperature variation of lesions are seen more frequently in EH than appocrine hydrocyctoma.[5]

Topical atropine or scopolamine,[6] incisions and drainage,[5] carbon dioxide laser and pulsed dye lasers[7] and flash lamp-pumped pulsed dye with a 585-nm laser[8] are modalities suggested for treatment of multiple EH.

Intradermal injection of botulinum toxin type-A (BT-A) has been reported as treatment of multiple EH in numbers of previous studies.[9-13]

This study was performed to evaluate usefulness of BT-A which was injected intrademally in multiple EH.

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MATERIALS AND METHODS

In this clinical trial study, 22 patients (16 females and 6 males) with clinically diagnosed and histopatholocically confirmed multiple EH aged 28-69 years referred to our clinic from 2006 to 2011 were enrolled.

Patients were divided into two groups nonrandomly based on the number of lesions: the first group included 12 patients (8 females and 4 males) and the second group included 10 patients (8 females and 2 males). The lesions often were observed in cheek, periorbital region and less commonly in forehead, nose, chin and upper lip area. In all patients thyroid hormone tests were normal. Half an hour exposure to relatively warm environment or a mild physical exercise was suggested to patients to make their lesions developed and prominent.

In the present study, vial of BT-A (Dysport; Ipsen Ltd, Slough, UK) containing 500 units, dissolved in 5 and 10 ml normal saline was suggested for treatment of multiple EH. With consent of the patients, BT-A at concentrations of 5 and 10 units in 0.01 ml were used in the first and second groups respectively.

Topical lidocain-prilocain was applied for local anesthesia. Insulin syringe with a 30-gauge needle was used for injection. Dependent on size and density of lesions variable volumes of BT-A were injected intradermally. If the lesions had more than 5mm (Fig. 1a) of diameter, 0.02-0.03cc of BT-A were injected intradermally perilesional. If lesions were numerous and discrete with diameter of less than 5mm (Fig. 2a), 0.02ml was injected intradermally, whereas if lesions were multiple and confluent (Fig. 3a), 0.02ml was injected intradermally in each 1cm.[2]

If lesions were numerous, especially those suited in periorbital and upper lip area, injection should have been performed cautiously to avoid probable complications.

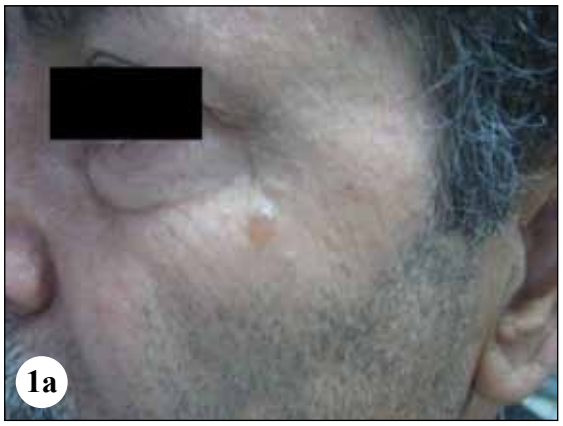

Fig. 1a Pretreatment multiple discrete lesions and a large lesion in cheek and periorbital area.

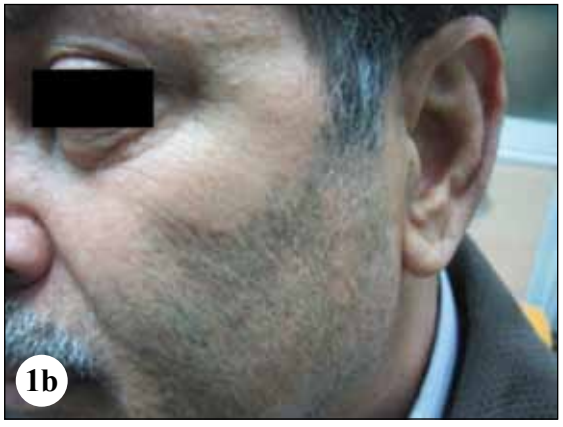

Fig. 1b Post-treatment.

Patients were followed according to the probable complications and to evaluate patients' improvement at the end of the second week, first, third, sixth and twelfth month. Assessment of improvement was based on disappearance of lesions before and after treatment by photography. If majority or all lesions subsided, the response was considered excellent, whereas if half to most of lesions improved it was considered as a good response.

Retreatment was performed for ignored or unresponsive lesions at the end of the second week in two patients who had numerous and diffuse lesions.

The proposal of the study was approved by the Ethics Committee of Kermanshah University of

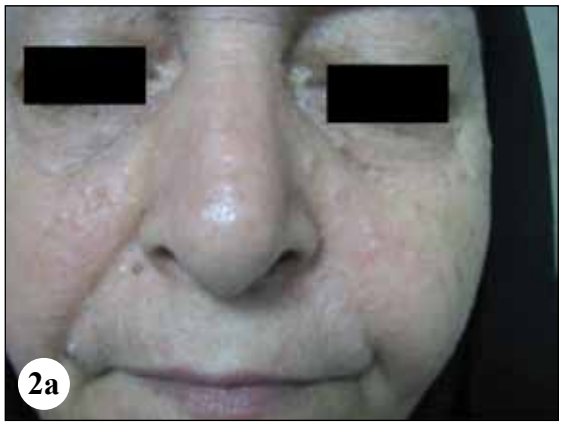

Fig. 2a Pretreatment with numerous lesions on the whole face.

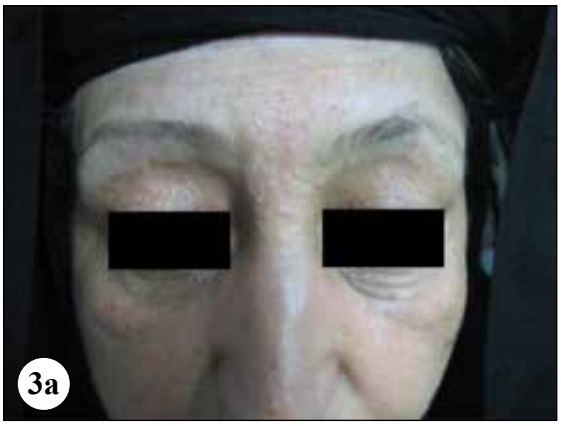

Fig. 3a pretreatment multiple and confluent lesions in glabella area.

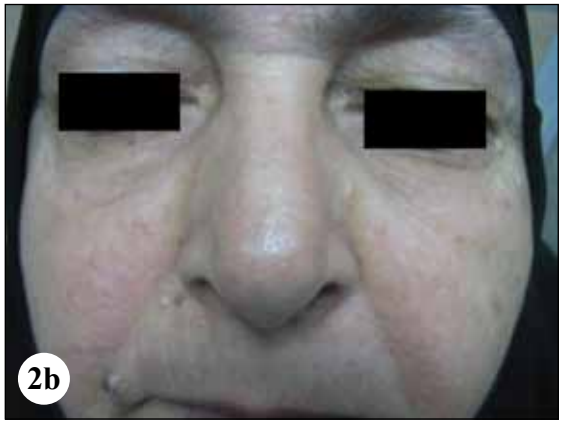

Fig. 2b After treatment.

Fig. 3b after treatment.

Medical Sciences and registered in IRCT database. In order to identify the difference between improvement of lesions and duration of BT-A in two groups Fisher's exact test was used.

RESULTS (Fig. 1-3a, b)

Seventy five percent of patients (9) in the first group and 80% of patients (8) in the second group had excellent response at the first session treatment. However, two patients showed significant improvement in retreatment at the end of second week (Table 1). No significant difference was observed between two groups in rate of clinical response (p value=0.727).

Duration of drug efficacy was 6-9 months in the first group with a mean time of 7.3 months and 6-8 months in the second group with a mean time of 6.9 months. No significant difference was detected between two groups regarding mean duration time (p value=0.840) (Table 2).

Ecchymosis was seen in all patients in both groups but it was severe in patients who had numerous and periorbital lesions. Two patient in both group showed asymmetric smile that improved spontaneously between 2-3 weeks. Other complication such as headache, belpharoptosis was not seen in any patients.

DISCUSSION

This study showed that BT-A is an effective drug for treatment of multiple EH. Two different doses of BT-A were used in our patients in both groups. No significant difference was seen between these two groups in clinical response rate

Table 1 Comparison of improvement at first session treatment in two groups

			Group		Total
Improvement			**I**	**II**	
	Good	Count	3	2	5
		%	25.0%	20.7%	22.7%
	Excellent	Count	9	8	17
		%	75.0%	80.0%	77.3%
Total		Count	12	10	22
		%	100.0%	100.0%	100.0%

Table 2 Comparisian of age and mean time of efficacy in two groups

	group	**N**	**Mean**	**Std. Deviation**	**P value**
age	I	12	45.60	15.209	.895
	II	10	46.83	14.784	
duration	I	12	7.32	1.304	.840
	II	19	6.93	.816	

(p value=0.727).

Mean time of drug efficacy was 7.3 and 6.9 months in the first and second groups respectively. There was no significant difference between two groups in mean duration time (p value=0.840) (Table 2).

BT-A induced side effects were mild and transient such as ecchymosis. Besides, one patient in each group showed asymmetric smile. This complication was seen in those who had numerous and diffuse EH lesions and was resolved spontaneously during 2-3 weeks.

Topical atropine and scopolamine were used for treatment of multiple EH in one of the previous studies but complications caused the patients to discontinue the treatment.[6]

Incision and drainage have been suggested for treatment of multiple EH but recurrence occurred after 6 weeks.[5]

Bickley et al. used Co2 laser for treatment of multiple apocrine hidrocyctoma but this modality might result in scar formation and its long time outcome is not clear.[14]

Although efficacy of pulsed dye laser with 585 nm has been reported previously for treatment of multiple EH,[8] another report showed this modality to be unsuccessful.[15]

BT-A has inhibitory effect in both motor and autonomic terminals by a similar mechanism which is inhibition of calcium-dependent neurotransmitter release. The autonomic inhibitory effect can result in its successful treatment in conditions such as hyperhidrosis.[16] It is hypothesized that BT-A results in disappearance of skin lesions in multiple EH with a similar mechanism.

Blugerman et al applied BT-A in a man with excellent result. Within 6 months no lesions were observed.[9] Correia et al used BT-A in two women and concluded that this drug is the first line treatment of multiple EH.[10] Furthermore, Liu et al used BT-A successfully in two Taiwanian women[11]. Woolery-Lioyd et al treated a 38-year-old-black woman with multiple EH in periorbital region with BT-A which showed disappearance of lesions after within 4 months.[12]

In one of previous studies including 17 patients 0.1-0.2ml of prepared solution containing 6.6 U in 0.01ml was injected intradermaly perilesional.[13] However, 0.02-0.03ml of BT-A (Dysport) solution containing 5 or 10 U in 0.01ml was used in current study which is about 0.1 dose of the mentioned study.

In conclusion, BTX-A has rapid and significant efficacy in treatment of multiple EH in spite of its mild and transient complications. Nevertheless, the necessity of repeated treatment every 6-12 months is the most important limitation of this drug. In addition, the rarity of this disease and the willingness of limited number of patients for this kind of treatment which results in the low number of cases are other limitations of the study.

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