Efficacy of Botulinum Toxin A in Preventing Recurrence Keloids: Double Blinded Randomized Controlled Trial Study: Intraindividual Subject

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Background: *Keloids have been one of the most concerning problems in cosmetic surgery. Current treatments still provide unpredictable outcomes. Interestingly, one molecular study of Botulinum Toxin A (BTXA) has found the inhibitive effect of fibroblast growth factor (TGF-β), which explain the mechanism of keloid formation.*
Objective: *To study the efficacy of BTXA in preventing keloids formation for clinical use.*
Material and Method: *Prospective randomized controlled trial study was conducted on 25 patients between March 2014 and June 2015. Fifty keloids from 25 patients were equally randomized into two groups, control and toxin group. After the scar excision, the control group was injected with corticotherapy, while the toxin group was injected with BTXA. The outcomes were assessed and evaluated using Vancouver Scar Scale (VSS) by two plastic surgeons. The VSS was compared between pre- and post-operative period. Follow-up protocols were made in both groups at 1-, 3-, and 6-month after surgery.*
Results: *According to the first and third-month follow-up, the outcome in toxin group was more favorable than the control group (6.22±1.72 vs. 5.89±1.83, p = 0.347), whereas the outcome in control group was more favorable than the toxin group in the sixth month follow-up (5.33±1.87 vs. 4.11±1.96, p = 0.010).*
Conclusion: *BTXA is not significantly better in preventing recurrence keloids when compared to corticotherapy after one and three months. However, Corticotherapy provides a significantly better outcome than BTXA at 6-month follow-up.*

Keyword: *Keloid, Botulinum toxin A, Corticotherapy*

J Med Assoc Thai 2017; 100 (3): 280-6
Full text. e-Journal: *http://www.jmatonline.com*

Keloids were first discussed by Alibert in 1806. They may result from a variety of cutaneous injuries, inflammatory disorders, burns, trauma, or iatrogenic surgical insult[1]. Keloids can be differentiated from hypertrophic scars in that excessive scar tissue proliferates beyond the limits of the original lesion[2,3] and do not regress over time[1-4].

Keloids and hypertrophic scars affects 30 to 90% of patients, and are characterized by pathologically excessive dermal fibrosis and aberrant wound healing[5]. Both entities have different clinical and histochemical characteristics, and unfortunately still represent great challenge for clinicians due to lack of efficacious treatments. Current advances in molecular biology and genetics reveal new preventive and therapeutically options that represent a hope to manage this highly prevalent, chronic and disabling problem, with long-term beneficial outcomes and improvement of quality of life[6-8]. However, we must wait for these innovative clinical products to be marketed. In the meantime, it is imperative to know the basics of the currently existing wide array of strategies to deal with excessive scars, from the classical corticotherapy, to the most recent Botulinum Toxin and lasers[1,5,8].

Unexpected outcome of keloid treatments is one of major problems in medical procedures, as available treatments do not achieve satisfactory results. A recent study has found the impairment in repaired process with TGF-β molecular mechanism in hypertrophic scar and keloid formation[9-14].

Botulinum Toxin Type A (BTXA) is now widely used in many medical indications such as neurological diseases[15-19], cosmetic conditions, or muscle paralysis effects[20-24]. A recent molecular study showed that BTXA can inhibit connective tissue Growth Factor Expression in fibroblast[25]. Dose dependent effects were compared in two groups, 49.2% (1U/106 cells) and 56.9% (2.5 U/106 cells) in the treatment groups.

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A review study of BTXA to prevent widening scar suggested that there was a 90% improvement in the outcome of the treatment group[26]. Mechanism was explained by muscle immobilization.

The efficacy of BTXA in prevention of keloid recurrence after surgical excision has never been reported. The objective was to compare efficacy between corticotherapy and BTXA in prevention recurrence of keloid after surgical excision.

Material and Method

Approval of the present study was obtained from the Ethics Committee of Phramongkutklao Hospital and College of Medicine. A prospective, randomized controlled trial was conducted between March 2014 and June 2015. Our protocol had been reviewed by TRTC with identification number is TCTR20150811002. Patients presented with keloid problems in our institute were included. The inclusion criteria were age over 18 years old, had at least two sites or one site longer than 10 cm in length, and had unsightly scars that required scar revision or excision. The exclusion criteria were allergic to Botulinum Toxin or lidocaine, pregnancy or during breast-feeding, received an injection of Botulinum Toxin within six months, undesirable medical conditions, and taking anticoagulant or antiplatelet drugs.

The patients' two scar sites were marked as "a" and "b", and scar lesions were equally randomized in two groups, toxin group, and control group. All patients enrolled for scar excision procedure. The scars were excised under local anesthesia injection (1% lidocaine with adrenaline) and primary wound closure were performed with subcuticular suture technique (vicryl 5-0). In tension areas, the skin was closed with nylon 6-0 (simple suture stitches).

In control group, the scars were injected with Triamcinolone acetonide (TA) (10 mg/cc) seven days after stitch removal. Dose of injection depended on size of wound, injected until skin wheel occurred, then the injection was repeated in the first, second and third month. In toxin group, the scars were injected with BTXA intradermal, with dose 1.5 units/1 cm in length (Botox® 50 units of toxin with 0.9% NSS for injection 2.5 cc, concentration 2 units per 0.1 cc) seven days after stitch removal (one dose). Patient, surgeon, and assessor were blinded from protocol procedure.

Follow-up protocols were performed at 7-day (for initial injection), at 14-day (for observation after injection treatment), at the 1-month (for observation and the second dose of injection in the control group), at the 3-month (for observation and the third dose of injection in the control group), and at 6-month (for observation and the fourth dose of injection in the control group). Assessor exam and scored all subjects in outpatient department on follow-up date.

The data collection included age, sex, treatment delay, cause of lesion, wound length, and location at the initial pre-operation with pre-operative and post-operative photographs.

Two plastic surgeons assessed surgical scar by using Vancouver Scar Scale (VSS) at pre-operative period, during the 1-, 3-, and 6-month. The surgeons were blinded during the evaluation. Mean result of VSS assessed from two plastic surgeons and analyzed in four characteristics: pigmentation, vascularity, pliability, and height (score from 0 to 13).

Statistical analysis

Data were analyzed with descriptive statistics for demographic data, paired t-test for VSS in the pre-operative at 1-, 3-, and 6-month. Probability of less than 0.05 was accepted as statistically significant. The software used was program SPSS version 20.

Results

Twenty-five patients were initially enrolled in the study. There were 10 females and 15 males. Average age was 26.40±6.98 years (Table 1). No statistically significant difference was found in mean pre-operative VSS between the two groups (9.22±2.39). There was improvement of VSS in both groups after injections at 1-, 3-, and 6-month. At 1- and 3-month follow-up, mean VSS in the toxin group was better

Table 1. Demographic data

	n (%)
Sex	
Male	10 (40.00)
Female	15 (60.00)
Age	
Mean ± SD	26.40±6.98
Median (min to max)	26 (18 to 49)
Dosage of botulinum toxin [units (for toxin site)], mean ± SD	18.05±5.54
Site of lesion	
Earlobe	10 (66.67)
Chest wall	2 (13.33)
Extremity	3 (20.00)
Cause of keloid	
Ear piercing	10 (66.67)
Post-surgery	5 (33.33)

Table 2. Compared VSS between group

	Controlled group		Toxin group		*p*-value*
	Mean ± SD	Median (min to max)	Mean ± SD	Median (min to max)	
Pre-operative					N/A
Vascularity	9.15±1.86	10 (4 to 12)	9.15±1.86	10 (4 to 12)	
Pigmentation	9.34±2.55	9 (5 to 12)	9.34±2.55	9 (5 to 12)	
Thickness	9.19±2.35	11 (4 to 11)	9.19±2.35	11 (4 to 11)	
Pliability	9.20±2.80	11 (4 to 12)	9.20±2.80	11 (4 to 12)	
Sum	9.22±2.39	10 (4 to 12)	9.22±2.39	10 (4 to 12)	
1-month					0.347
Vascularity	3.30±1.43	3 (2 to 6)	3.18±1.00	3 (2 to 5)	
Pigmentation	3.28±1.00	4 (2 to 5)	2.80±1.25	2 (2 to 5)	
Thickness	3.49±2.25	3 (2 to 6)	3.09±1.20	3 (2 to 5)	
Pliability	3.25±1.32	3 (2 to 5)	2.93±1.03	2 (2 to 5)	
Sum	3.33±1.50	3 (2 to 6)	3.00±1.12	3 (2 to 5)	
3-month					0.086
Vascularity	3.49±2.34	3 (2 to 5)	4.41±2.00	4 (2 to 6)	
Pigmentation	3.60±1.54	4 (2 to 6)	4.60±1.31	5 (2 to 7)	
Thickness	3.70±1.36	3 (2 to 5)	4.58±1.12	4 (3 to 7)	
Pliability	2.53±1.40	3 (2 to 6)	4.65±1.25	5 (2 to 7)	
Sum	3.67±1.66	3 (2 to 6)	4.56±1.42	5 (2 to 7)	
6-month					0.010
Vascularity	3.85±2.20	3 (2 to 7)	5.05±1.07	5 (4 to 7)	
Pigmentation	3.95±1.34	4 (3 to 7)	5.15±1.22	4 (5 to 7)	
Thickness	3.84±2.04	3 (2 to 7)	5.08±1.33	5 (4 to 7)	
Pliability	3.92±1.46	3 (3 to 7)	5.16±0.10	5 (4 to 7)	
Sum	3.89±1.76	3 (2 to 7)	5.11±0.93	5 (4 to 7)	

VSS = Vancouver Scar Scale; NA = not applicable
* Paired t-test

than control group (3.00±1.12 vs. 3.33±1.50, $p = 0.347$) and (3.67±1.66 vs. 4.56±1.42, $p = 0.086$). At 6-month follow-up, mean VSS in the control group (3.89±1.76) was better than the toxin group (5.11±0.93) (Table 2). Statistical significance of VSS was found between pre-operative and post-operative within groups (Table 3).

Cases example

Case 1

A 20-year-old male presented with keloids on both earlobes after he had ears pierced three years ago. Right lesion was assigned to the toxin group, while left lesion was control group. Pre-operative result was compared to 6-month post-operative result (Fig. 1).

Case 2

A 33-year-old female presented with keloids on both earlobes after she had ears pierced one year before. Right lesion was assigned to the control group, while left lesion was the toxin group. Pre-operative result was compared with 6-month post-operative result (Fig. 2).

Table 3. Compared VSS within group

	Mean ± SD	Median (min to max)	*p*-value*
Control			
Pre-operative	9.22±2.39	10 (4 to 12)	
1-month	3.33±1.50	3 (2 to 6)	<0.001
3-month	3.67±1.66	3 (2 to 6)	<0.001
6-month	3.89±1.76	3 (2 to 7)	<0.001
Toxin			
Pre-operative	9.22±2.39	10 (4 to 12)	
1-month	3.00±1.12	3 (2 to 5)	<0.001
3-month	4.56±1.42	5 (2 to 7)	<0.001
6-month	5.11±0.93	5 (4 to 7)	<0.001

Paired t-test compared with pre-operative

Discussion

There are many protocols to inject TA such as prior excision, intraoperative or post-operative, and monthly interval. In the present study, we injected TA at 1-week after excision according to the of Donkor[27] and Narakula and Shenoy[28]. TA was injected on postoperative day 7 to inhibit fibroblast function in the proliferative phase after completion of inflammatory phase of wound healing.

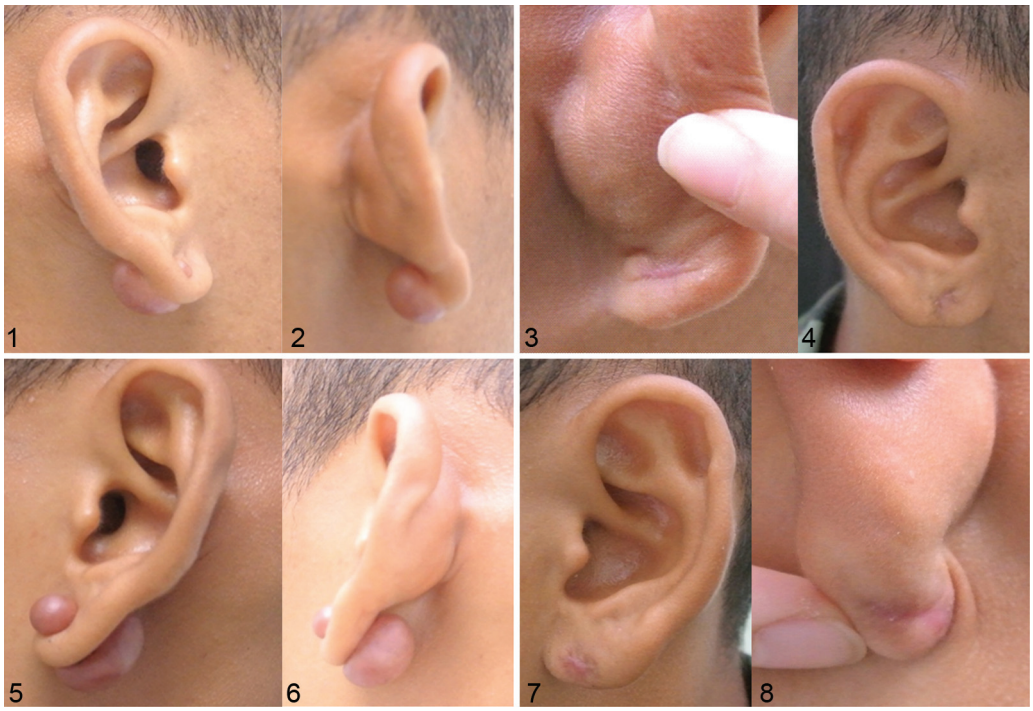

Fig. 1 A 20 year-old male was presented with keloids on both earlobes after he had ears pierced 3 years ago. Right lesion was assigned to the toxin group, while left lesion was the controlled group. Pre-operative result was compared to post-operative 6-month result. Mark: 1-2 = toxin group pre-operative (right ear); 3-4 = toxin group post-operative 6-month (right ear); 5-6 = controlled group pre-operative (left ear); 7-8 = controlled group post-operative 6-month (left ear).

The present study was different from other studies as it did not compare the results with placebo treatment. This study compared head to head with corticotherapy, which had already been proved to have positive result when compared to placebo. Previous study dealt with widening scars with intramuscular injection and studied chemo-immobilized effect[29-33]. The present study considered the inhibitive effect of fibroblast growth factor (TGF-β), so, we performed intradermal injection, because fibroblast are main in dermis.

From our results, post-operative injection with BTXA to prevent keloids recurrence achieved better outcome in the short-term follow-up (1- to 3-month), but was not more favorable than the corticotherapy intradermal injection after six months. The long-term result in the control group that showed superior effect over the toxin group may be due to difference of each treatment times of two groups. Corticotherapy injection was repeated dose in the control group after the first month follow-up, while the toxin group did not receive repeated doses. This is because the standard protocol of corticotherapy call for repeating the dose every month. Normally, intramuscular injection will lengthen the effect of BTXA for three to four months after the first injection; the intradermal injection in the present study may not yield the same result as intramuscular injection.

Advantage of the present study was that the study had two procedures, control and toxin on the same subject. Because we know keloid are multifactorial risks, same subject can decrease personal factor and make result more accurate.

Effect of BTXA on prevention recurrence of keloids is a preventive effect like corticotherapy. Therefore, it should have benefit comparing to placebo because of corticotherapy are widely accepted in preventive effect. Herein, BTXA can be chosen as an alternative method in keloids prevention with less pain on injection due to neutral solution and lower frequency. BTXA can reduce chance of scar depression, which is one of the common sequalae of corticosteroid over used or over dosed. Steroid can make subcutaneous fat and dermis around keloid shrink if the solution spread out from the lesion or scar during injection. The reason that long-term follow-up corticotherapy showed

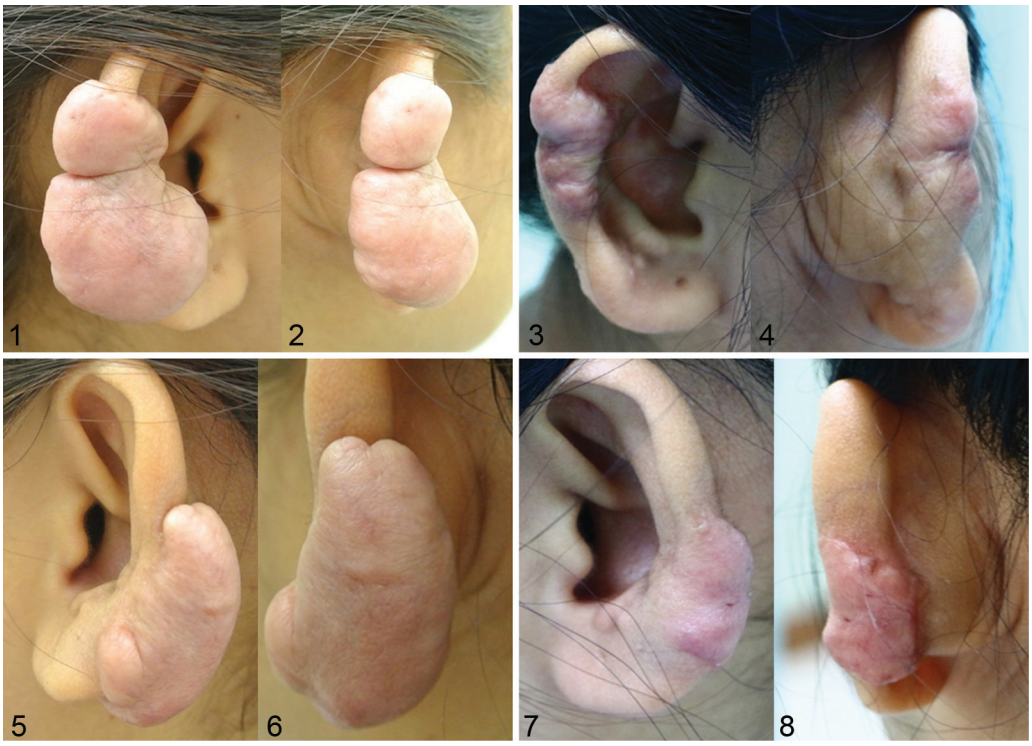

Fig. 2 A 33 year-old female presented with keloids on both earlobes after she had ears pierced for 1 year. Right lesion was assigned to the controlled group, while left lesion was the toxin group. Pre-operative result was compared to 6-month post-operative result. Mark: 1-2 = controlled group pre-operative (right ear); 3-4 = controlled group pre-operative (right ear); 5-6 = toxin group pre-operative (left ear); 7-8 = toxin group post-operative 6-month (left ear).

superior effect than BTXA in keloid formation may be due to infection as corticotherapy had more injection than BTXA, which had only once. From the result in short-term follow-up, the BTXA had also equal VSS. This can be assumed that at the same period, if given two injections, BTXA could provide similar result. The present study used dosage of BTXA as 1.5 units/1 cm, which referred to the study of Wilson[26]. Further study, should increase dosage of BTXA injection and times of injection if we would like to improve the treatment outcomes.

The limitation of the present study is the low number of subject, which is only 15 subjects. This may be too low to show power of differentiation. Additionally, the distribution of lesion did not have any variation as all lesions were earlobes (10 cases).

Conclusion

BTXA was not better in preventing recurrence keloids as compared to corticotherapy at 1- and 3-month. Corticotherapy can provided better significant outcome than BTXA at 6-month follow-up.

What is already known on this topic?

A review study of BTXA to prevent widening scar suggested that there was a 90% improvement in the outcome of the treatment group[26]. Mechanism was explained by muscle immobilization. One molecular study of BTXA has found the inhibitive effect of TGF-β, which explain the mechanism of keloid formation.

The efficacy of BTXA in prevention of keloid recurrence after surgical excision has never been reported.

What this study adds?

BTXA can be used to prevent of recurrence keloid formation as effective as corticotherapy at 3-month follow-up. The advantage of using BTXA is a single injection as compared to corticotherapy, which requires monthly injection.

Patient consent

All patients provided written consent for the use of their images.

Acknowledgement

The authors would like to thank Mrs. Supak Cae-ngow, statistician and the research assistant of the Office of Research Development, Phramongkutklao College of Medicine for her kind help in the statistical analysis of this article.

Potential conflicts of interest

None.

References

1. Berman B, Bieley HC. Keloids. J Am Acad Dermatol 1995; 33: 117-23.
2. Peacock EE Jr, Madden JW, Trier WC. Biologic basis for the treatment of keloids and hypertrophic scars. South Med J 1970; 63: 755-60.
3. Mancini RE, Quaife JV. Histogenesis of experimentally produced keloids. J Invest Dermatol 1962; 38: 143-81.
4. Rockwell WB, Cohen IK, Ehrlich HP. Keloids and hypertrophic scars: a comprehensive review. Plast Reconstr Surg 1989; 84: 827-37.
5. Mustoe TA, Cooter RD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, et al. International clinical recommendations on scar management. Plast Reconstr Surg 2002; 110: 560-71.
6. Leventhal D, Furr M, Reiter D. Treatment of keloids and hypertrophic scars: a meta-analysis and review of the literature. Arch Facial Plast Surg 2006; 8: 362-8.
7. Bombaro KM, Engrav LH, Carrougher GJ, Wiechman SA, Faucher L, Costa BA, et al. What is the prevalence of hypertrophic scarring following burns? Burns 2003; 29: 299-302.
8. Gauglitz GG, Korting HC, Pavicic T, Ruzicka T, Jeschke MG. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Mol Med 2011; 17: 113-25.
9. Wolfram D, Tzankov A, Pulzl P, Piza-Katzer H. Hypertrophic scars and keloids--a review of their pathophysiology, risk factors, and therapeutic management. Dermatol Surg 2009; 35: 171-81.
10. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. Wound Rep Reg 2008; 16: 585-601.
11. Atiyeh BS, Costagliola M, Hayek SN. Keloid or hypertrophic scar: the controversy: review of the literature. Ann Plast Surg 2005; 54: 676-80.
12. Marneros AG, Krieg T. Keloids--clinical diagnosis, pathogenesis, and treatment options. J Dtsch Dermatol Ges 2004; 2: 905-13.
13. Ashcroft KJ, Syed F, Bayat A. Site-specific keloid fibroblasts alter the behaviour of normal skin and normal scar fibroblasts through paracrine signalling. PLoS One 2013; 8: e75600.
14. Baum CL, Arpey CJ. Normal cutaneous wound healing: clinical correlation with cellular and molecular events. Dermatol Surg 2005; 31: 674-86.
15. Simpson DM, Gracies JM, Graham HK, Miyasaki JM, Naumann M, Russman B, et al. Assessment: Botulinum neurotoxin for the treatment of spasticity (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008; 70: 1691-8.
16. McCrory P, Turner-Stokes L, Baguley IJ, De Graaff S, Katrak P, Sandanam J, et al. Botulinum toxin A for treatment of upper limb spasticity following stroke: a multi-centre randomized placebo-controlled study of the effects on quality of life and other person-centred outcomes. J Rehabil Med 2009; 41: 536-44.
17. Karp BI, Cole RA, Cohen LG, Grill S, Lou JS, Hallett M. Long-term botulinum toxin treatment of focal hand dystonia. Neurology 1994; 44: 70-6.
18. Hoare BJ, Wallen MA, Imms C, Villanueva E, Rawicki HB, Carey L. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). Cochrane Database Syst Rev 2010; (1): CD003469.
19. Costa J, Espirito-Santo C, Borges A, Ferreira JJ, Coelho M, Moore P, et al. Botulinum toxin type A therapy for cervical dystonia. Cochrane Database Syst Rev 2005; (1): CD003633.
20. Carruthes A, Carruthers J. The use of botulinum toxin to treat glabellar frown lines and other facial wrinkles. Cosmet Dermatol 1994; 7: 11-15.
21. Garcia A, Fulton JE Jr. Cosmetic denervation of the muscles of facial expression with botulinum toxin: a dose response study. Dermatol Surg 1996; 22: 39-43.
22. Carruthers JD, Carruthers JA. Treatment of glabellar frown lines with C. botulinum-A exotoxin. J Dermatol Surg Oncol 1992; 18: 17-21.
23. Weiss JS, Ellis CN, Headington JT, Voorhees JJ. Topical tretinoin in the treatment of aging skin. J Am Acad Dermatol 1988; 19: 169-75.
24. Keen M, Blitzer A, Aviv J, Binder W, Prystowsky J, Smith H, et al. Botulinum toxin A for hyperkinetic

facial lines: results of a double-blind, placebo-controlled study. Plast Reconstr Surg 1994; 94: 94-9.
25. Xiao Z, Zhang M, Liu Y, Ren L. Botulinum toxin type a inhibits connective tissue growth factor expression in fibroblasts derived from hypertrophic scar. Aesthetic Plast Surg 2011; 35: 802-7.
26. Wilson AM. Use of botulinum toxin type A to prevent widening of facial scars. Plast Reconstr Surg 2006; 117: 1758-66.
27. Donkor P. Head and neck keloid: treatment by core excision and delayed intralesional injection of steroid. J Oral Maxillofac Surg 2007; 65: 1292-6.
28. Narakula GK, Shenoy RK. A prospective clinical review of "multi model" approach for treating ear keloids. Indian J Plast Surg 2008; 41: 2-7.
29. Xiaoxue W, Xi C, Zhibo X. Effects of botulinum toxin type A on expression of genes in keloid fibroblasts. Aesthet Surg J 2014; 34: 154-9.
30. Kim YS, Hong JW, Yoon JH, Hwang YS, Roh TS, Rah DK. Botulinum toxin A affects early capsule formation around silicone implants in a rat model. Ann Plast Surg 2015; 74: 488-95.
31. Wilson AM. Eradication of keloids: Surgical excision followed by a single injection of intralesional 5-fluorouracil and botulinum toxin. Can J Plast Surg 2013; 21: 87-91.
32. Gauglitz GG, Bureik D, Dombrowski Y, Pavicic T, Ruzicka T, Schauber J. Botulinum toxin A for the treatment of keloids. Skin Pharmacol Physiol 2012; 25: 313-8.
33. Haubner F, Leyh M, Ohmann E, Sadick H, Gassner HG. Effects of botulinum toxin A on patient-specific keloid fibroblasts in vitro. Laryngoscope 2014; 124: 1344-51.

ประสิทธิผลของ โบทูลินั่ม ท็อกซิน เอ ในการป้องกันการเกิดเป็นซ้ำของแผลเป็นคีลอยด์: การทดลองแบบสุ่มชนิดปิดในบุคคลเดียวกัน

ชาติชาย พฤกษาพงษ์, ศริปรียา ยิ่งทวีสิทธิกุล, ชัยรัตน์ บุรุษพัฒน์

ภูมิหลัง: *การรักษาแผลเป็นคีลอยด์ เป็นปัญหาที่สำคัญอย่างหนึ่งในการรักษาเรื่องความสวยงาม การรักษาในปัจจุบันยังให้ผลที่ไม่แน่ชัด มีการศึกษาก่อนหน้านี้ว่า โบทูลินั่ม ท็อกซิน เอ สามารถยับยั้งการสร้างไฟโบรบลาสโกรทแฟคเตอร์ (TGF-B) ซึ่งอธิบายการเกิดแผลเป็นคีลอยด์ได้*

วัตถุประสงค์: *เพื่อดูประสิทธิผลการป้องกันการเกิดแผลเป็นคีลอยด์ด้วยสารโบทูลินั่ม ท็อกซิน เอ ในทางเวชปฏิบัติ*

วัสดุและวิธีการ: *การศึกษาในผู้ป่วยที่ได้รับการวินิจฉัยเป็นแผลเป็นคีลอยด์ และได้รับการผ่าตัดแก้ไขจำนวน 25 ราย ณ โรงพยาบาลพระมงกุฎเกล้า ระหว่างเดือน มีนาคม พ.ศ. 2557 ถึง มิถุนายน พ.ศ. 2558 โดยหลังผ่าตัดผู้ป่วยจะได้รับการแบ่งแผลออกเป็น 2 ส่วน และได้รับการฉีดรักษาแบบสุ่มชนิดปิดด้วยโบทูลินั่ม ท็อกซิน เอ และคอร์ติโคสเตียรอยด์ และติดตามผลการรักษาเพื่อเปรียบเทียบการกลับเป็นซ้ำที่ระยะเวลา 1 เดือน 3 เดือน และ 6 เดือน*

ผลการศึกษา: *ผลการรักษาพบว่า กลุ่มที่ใช้การรักษาด้วย โบทูลินั่ม ท็อกซิน เอ ได้ผลดีกว่ากลุ่มที่ใช้คอร์ติโคสเตียรอยด์ (6.22±1.72 vs. 5.89±1.83, p = 0.347) ในระยะ 1 และ 3 เดือน ของการรักษา แต่ในระยะ 6 เดือน กลุ่มที่รักษาด้วยคอร์ติโคสเตียรอยด์จะได้ผลดีกว่า (5.33±1.87 vs. 4.11±1.96, p = 0.010)*

สรุป: *การรักษาการเกิดเป็นซ้ำในการรักษาแผลเป็นคีลอยด์ด้วยโบทูลินั่ม ท็อกซิน เอ ได้ผลดีกว่าคอร์ติโคสเตียรอยด์ในระยะ 1 และ 3 เดือน หลังการรักษา แต่ในระยะ 6 เดือน การรักษาด้วยคอร์ติโคสเตียรอยด์จะได้ผลดีกว่าอย่างมีนัยสำคัญ*
