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A comparative study of Botulinum toxin type A versus conventional oral therapy as a second-line treatment of diabetic neuropathy

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Abstract

Background: Diabetes mellitus is commonly complicated by diabetic peripheral neuropathy. Poor adherence to medication is common in diabetic peripheral neuropathy mainly due to common side effects and poor tolerance to medication. Botulinum toxin A intradermal injection has proved efficacy in cases of diabetic peripheral neuropathy, however there is a need to compare its effect to other lines of treatment. The aim of the study was to compare Botulinum toxin type A versus conventional oral treatment as a second-line treatment of painful diabetic peripheral neuropathy. The current study was a comparative study on 30 patients with type 2 diabetes mellitus. Diabetic peripheral neuropathy was proved by nerve conduction study. All patients were on carbamazepine. Patients were divided randomly into three groups. First group was add-on duloxetine, second group was add-on gabapentin and the third group was injected intradermal with Botulinum toxin A.

Results: Our study showed that Botulinum A intradermal injection, gabapentin and duloxetine add-on therapy decreased the VAS and PSQI over a 12-week study period and this was statistically significant at $p < 0.001$*. Botulinum A intradermal injection also decreased the mean of PSQ1 from 17.3 ± 1.8 to 10.9 ± 3.1 in 12 weeks constituting the highest decline in PSQ1 among the three groups and this was statistically significant at $p < 0.001$*.

Conclusion: Botulinum toxin A injection had a comparable if not superior efficacy to duloxetine and gabapentin as a second-line treatment of diabetic peripheral neuropathy.

Keywords: Diabetes, Peripheral neuropathy, Botulinum toxin A

Background

Diabetes mellitus is commonly complicated by diabetic peripheral neuropathy and its prevalence is approximately 60–70% among 347 million people with diabetes mellitus worldwide [1]. Neuropathic pain is a frequent companion to diabetic peripheral neuropathy [2].

Various pain medications such as antidepressants, anticonvulsants, topical agents and opioids have been evaluated in people with diabetic peripheral neuropathy [3, 4]; however, because of the common side effects [3, 5] and poor adherence to medication there is a need of new lines of treatment [5].

Complications of diabetic peripheral neuropathy include paraesthesia, sensory loss and subsequent ulcers, osteomyelitis, deformities, gangrene and, ultimately, foot amputation; therefore, new therapeutic approaches are needed to reduce neuropathic symptoms and improve the outcome in people with diabetic peripheral neuropathy [5, 6].

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Botulinum neurotoxins (BTX-A) are used in treatment of spasticity and glandular hyperactivity but also found to suppress both nociceptor sensitization and neuropathic pain such as trigeminal neuralgia and carpal tunnel syndrome [7, 8].

In a systemic review done by Chengbing Wang and colleagues [9] in 2021, they showed that reducing pain in diabetic peripheral neuropathy by Botulinum A toxin can be safe and effective. This systemic review was done comparing only four studies, which emphasis the need to study the effect of Botulinum A in diabetic peripheral neuropathy. The current study aimed to compare Botulinum toxin type A with conventional oral treatment as a second-line treatment of painful diabetic peripheral neuropathy.

Methods

The current study was a comparative study on 30 patients with type 2 diabetes mellitus. All patients suffered from diabetic peripheral neuropathy proved by nerve conduction study. All patients were on carbamazepine as a first-line treatment for diabetic peripheral neuropathy dose was 200 mg twice. Patients were divided randomly into three groups. First group was add-on duloxetine 60 mg once daily, second was add-on gabapentin 300 mg twice daily and the third group was injected intradermal with Botulinum toxin A.

Botulinum toxin was injected intradermal with a dose of 50 units in each foot intradermal evenly distributed equally in 10 injection sites.

Baseline and follow-up assessment were performed after adding second-line treatment (gabapentin, duloxetine and Botulinum toxin A) through visual analogue scale (VAS) and Pittsburgh Sleep Quality Index (PSQI) at 0, 1 week, 4 weeks, 12 weeks.

Inclusion criteria were type 2 diabetic patients on carbamazepine as a single line of treatment for neuropathic pain.

Exclusion criteria were any severe medical condition that might interfere with the results.

Informed consents written and oral were obtained from the patients to use their anonymous data for research purposes. Regarding statistical analysis of the data, data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). The Kolmogorov–Smirnov test was used to verify the normality of distribution of variables, comparisons between groups for categorical variables were assessed using Chi-square test (Monte Carlo). ANOVA was used for comparing the four studied groups and followed by post hoc test (Tukey) for pairwise comparison. Kruskal–Wallis test was used to compare different groups for abnormally distributed quantitative variables. ANOVA with repeated measures, compare different periods using post hoc test (adjusted Bonferroni). Significance of the obtained results was judged at the 5% level.

Results

This study was conducted on 30 diabetic patients with diabetic peripheral neuropathy on carbamazepine and they were divided in to three equal groups with add-on duloxetine gabapentin and intradermal Botox injection.

Table 1 shows the demographic and clinical characteristics of the studied groups. All three groups were matched regarding age and sex and duration of diabetes. Mean age was 59.5 years for duloxetine 58 years for gabapentin and 63 years in Botulinum toxin A group.

Table 1 Comparison between the three studied groups according to age, sex, diabetic medication and duration of diabetes

	Duloxetine ($n=10$)	Gabapentin ($n=10$)	Botox ($n=10$)	Test of sig	p
Sex					
Male	5 (50%)	4 (40%)	4 (40%)	$\chi^2=0.381$	$^{MC}p=1.000$
Female	5 (50%)	6 (60%)	6 (60%)		
Age (years)					
Mean ± SD	59.9 ± 7	59.1 ± 9.4	60.9 ± 9.8	$F=0.105$	0.900
Median (Min.–Max.)	59.5 (50–70.0)	58 (45–72)	62 (47–76)		
Medication					
Oral	6 (60%)	9 (90%)	8 (80%)	$\chi^2=2.400$	$^{MC}p=0.430$
Insulin	4 (40%)	1 (10%)	2 (20%)		
Duration (years)					
Mean ± SD	9.2 ± 6.4	6.4 ± 4.4	9.6 ± 6.2	$H=1.712$	0.425
Median (Min.–Max.)	7 (3–24)	5 (2–16)	9 (2–20)		

SD: standard deviation; χ^2: Chi-square test; *F*: *F* for ANOVA test; MC: Monte Carlo; *H*: *H* for Kruskal–Wallis test

p: *p* value for comparing between the three studied groups

With no statistically significant difference among the three groups at $p=0.900$.

Oral hypoglycemic drugs were the main line of treatment of diabetes in the studied groups. 60% of patients on oral hypoglycemic drugs in the duloxetine group 90% for gabapentin group and 80% in Botulinum toxin A group with no statistically significant difference among the three groups at $p=0.430$.

Regarding the duration of diabetes, mean duration of diabetes was 9.2 ± 6.4 years for duloxetine group 6.4 ± 4.4 years for gabapentin group and 9.6 ± 6.2 years in Botulinum toxin A group. With no statistically significant difference among the three groups at $p=0.425$.

Table 2 shows the VAS at 0, 1, 4, 12 weeks comparing duloxetine, gabapentin and Botulinum toxin A injection.

Baseline mean VAS was 8 ± 1.1 in the duloxetine group 7.5 ± 1.1 in the gabapentin and 8.1 ± 0.7 in the Botulinum toxin A group. There was no statistically significant difference among the three groups at $p=0.348$.

VAS decreased in the three groups, yet it was not a statistically significant difference between the three groups at $p=0.316$.

Table 3 and Figure 1 show that duloxetine, gabapentin and Botulinum toxin significantly decreased the VAS along week 0 to 12.

Duloxetine add-on therapy decreased the VAS from a mean of 8 ± 1.1 to 5.8 ± 0.9 after 12 weeks and this was statistically significant at $p<0.001$*

While gabapentin add-on therapy decreased the VAS mean from 7.5 ± 1.1 to a mean of 5.5 ± 1.1 after 12 weeks, this was statistically significant at $p<0.001$*

Botulinum A intradermal injection also decreased the mean of VAS from 8.1 ± 0.7 to 6.2 ± 1 in 12 weeks and this was statistically significant at $p<0.001$*

When comparing VAS 0 to VAS 1, 4, 12 among each patient group Botulinum toxin A was the only drug that caused statistically significant difference all along the study duration $p^1=0.019$*, <0.001*, 0.004*, respectively.

When comparing PSQ1 among different add-on therapy, Table 4 shows that baseline mean PSQ1 was 17.4 ± 2.21 in the duloxetine group 16.2 ± 2.7 in the gabapentin and 17.3 ± 1.8 in the Botulinum toxin A group with no statistically significant difference among the groups at $p=0.437$.

PSQ1 at week 4 was lowest in the Botulinum A intradermal group mean $=9.9\pm3.6$ and this was statistically significant at $p=0.001$*

This decline was confirmed even further when comparing duloxetine and gabapentin $p_1=0.891$ which was statistically insignificant.

p value when comparing duloxetine and Botox was $p_2=0.002$* which was statistically significant, p value when comparing between gabapentin and Botox was $p_3=0.005$* which was statistically significant.

Table 5 and Figure 2 show that duloxetine add-on therapy decreased the PSQ1 from a mean of 17.4 ± 2.2 to 13.8 ± 2.4 after 12 weeks and this was statistically significant at $p<0.001$*.

While gabapentin add-on therapy decreased the PSQ1 mean from 16.2 ± 2.7 to 13.3 ± 3 after 12 weeks, this was statistically significant at $p<0.001$*.

Botulinum A intradermal injection also decreased the mean of PSQ1 from 17.3 ± 1.8 to 10.9 ± 3.1 in 12 weeks

Table 2 Comparison between the three studied groups according to VAS

VAS	Duloxetine ($n=10$)	Gabapentin ($n=10$)	Botox ($n=10$)	*F*	*p*
VAS 0					
Mean ± SD	8 ± 1.1	7.5 ± 1.1	8.1 ± 0.7	1.098	0.348
Median (Min.–Max.)	8 (6–9)	7.5 (6–9)	8 (7–9)		
VAS 1 week					
Mean ± SD	7.5 ± 1.4	6.6 ± 1.6	7.3 ± 0.8	1.231	0.308
Median (Min.–Max.)	7.5 (6–9)	6.5 (4–9)	7.5 (6–8)		
VAS 4 weeks					
Mean ± SD	6.3 ± 1.2	5.7 ± 1.3	5.5 ± 0.8	1.431	0.257
Median (Min.–Max.)	6.5 (4–8)	6 (4–8)	5.5 (4–7)		
VAS 12 weeks					
Mean ± SD	5.8 ± 0.9	5.5 ± 1.1	6.2 ± 1	1.202	0.316
Median (Min.–Max.)	5.5 (5–7)	5 (4–8)	6 (5–8)		

SD: standard deviation

F: *F* for ANOVA test

p: *p* value for comparing between the three studied groups

Table 3 Comparison between the different studied periods according to VAS

VAS	VAS 0	VAS 1 week	VAS 4 weeks	VAS 12 weeks	*F*	*p*
Duloxetine ($n=10$)						
Mean ± SD	8 ± 1.1	7.5 ± 1.4	6.3 ± 1.2	5.8 ± 0.9	17.553*	< 0.001*
Median (Min.–Max.)	8 (6–9)	7.5 (6–9)	6.5 (4–8)	5.5 (5–7)		
p_1		1.000	< 0.001*	0.001*		
Gabapentin ($n=10$)						
Mean ± SD	7.5 ± 1.1	6.6 ± 1.6	5.7 ± 1.3	5.5 ± 1.1	9.108*	< 0.001*
Median (Min.–Max.)	7.5 (6–9)	6.5 (4–9)	6 (4–8)	5 (4–8)		
p_1		0.112	0.004*	0.009*		
Botox ($n=10$)						
Mean ± SD	8.1 ± 0.7	7.3 ± 0.8	5.5 ± 0.8	6.2 ± 1	30.221*	< 0.001*
Median (Min.–Max.)	8 (7–9)	7.5 (6–8)	5.5 (4–7)	6 (5–8)		
p_1		0.019*	< 0.001*	0.004*		

SD: standard deviation

F: *F* test (ANOVA) with repeated measures, Sig. bet. periods was done using post hoc test (adjusted Bonferroni)

p: *p* value for comparing between the different studied periods

p_1: *p* value for comparing between VAS 0 and each other period in each group

* Statistically significant at $p \leq 0.05$

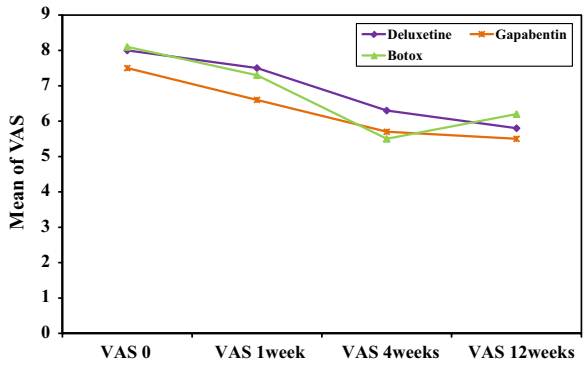

Fig. 1 Comparison between the different studied periods according to VAS

constituting the highest decline in PSQ1 among the three groups and this was statistically significant at $p < 0.001$*.

When comparing PSQ1 0 to of PSQ1 1, 4, 12 weeks among each patient group, Botulinum toxin A was the only drug that caused statistically significant difference all along the study duration, $p^1 = 0.016$**, < 0.001*, < 0.001**, respectively.

Discussion

In the current study, we compared 30 patients with diabetic peripheral neuropathy on carbamazepine, regarding add-on therapy. Duloxetine, gabapentin and intradermal Botulinum toxin A injection were compared in three groups (10 patients each) VAS and PSQ1 were compared at a 0, 1, 4, 12 weeks after initiation of add-on therapy. All three lines of treatment successfully decreased PSQI and VAS and this was statistically significant.

Botulinum toxin A caused the highest and fastest reduction in the VAS and PSQ1 compared to gabapentin and duloxetine.

In literature there is limited data about the effect of Botulinum a toxin injection in comparison with other lines of treatment.

Regarding the dose of Botulinum toxin A in the current study, we used 50 units intradermal injection this was in concordance with a study by Yuan and colleagues [10], but higher doses were used in other studies. In a study by Ghasemi and colleagues 100 units of BTX-A in one foot was used [11], while in another study by Salehi and colleagues 100 units of BTX-A was injected in each foot [12], while the study by Taheri injected 150 units of BTX-A intradermal in each foot [13].

In a study by Moon and colleagues [14], in 2016 they performed an ultrasound-guided Botulinum toxin type A (BoNT-A) injection in 2 cases with intractable post-herpetic neuralgia (PHN), painful diabetic neuropathy. Yet this study was not comparative with the effect of drugs due to patient's intolerance to side effect, also they only injected 2 patients, yet he reported significant improvement of pain for 5 months which was in concordance with our study.

In our study, we compared different add-on treatment options. Most of the studies were in comparison to placebo, for example in a randomized controlled trial by Eitner and colleagues [15] they showed that compared

Table 4 Comparison between the three studied groups according to PSQI

BISP	Duloxetine ($n=10$)	Gabapentin ($n=10$)	Botox ($n=10$)	*F*	*p*
PSQI 0					
Mean ± SD	17.4 ± 2.2	16.2 ± 2.7	17.3 ± 1.8	0.854	0.437
Median (Min.–Max.)	18 (14–20)	17.5 (12–19)	17.5 (15–20)		
PSQI 1 week					
Mean ± SD	16.7 ± 2.4	15.7 ± 2.6	15.9 ± 2.4	0.464	0.634
Median (Min.–Max.)	17 (14–20)	16.5 (11–19)	16 (12–20)		
PSQI 4 weeks					
Mean ± SD	15 ± 1.6	14.4 ± 3.2	9.9 ± 3.6	9.070*	0.001*
Median (Min.–Max.)	14.5 (13–18)	13.5 (9–20)	10 (6–16)		
Sig. bet. grps	$p_1=0.891$, $p_2=0.002^*$, $p_3=0.005^*$				
PSQI 12 weeks					
Mean ± SD	13.8 ± 2.4	13.3 ± 3	10.9 ± 3.1	2.915	0.071
Median (Min.–Max.)	13 (9–17)	13.5 (9–19)	11 (7–15)		

SD: standard deviation

F: *F* for ANOVA test, pairwise comparison bet. Each two groups was done using post hoc test (Tukey)

p: *p* value for comparing between the three studied groups

p_1: *p* value for comparing between duloxetine and gabapentin

p_2: *p* value for comparing between duloxetine and Botox

p_3: *p* value for comparing between gabapentin and Botox

* Statistically significant at $p \leq 0.05$

Table 5 Comparison between the different studied periods according to PSQI

PSQI	PSQI 0	PSQI 1 week	PSQI 4 weeks	PSQI 12 weeks	*F*	*p*
Duloxetine ($n=10$)						
Mean ± SD	17.4 ± 2.2	16.7 ± 2.4	15 ± 1.6	13.8 ± 2.4	32.863*	< 0.001*
Median (Min.–Max.)	18 (14–20)	17 (14–20)	14.5 (13–18)	13 (9–17)		
p_1		0.149	0.002*	< 0.001*		
Gabapentin ($n=10$)						
Mean ± SD	16.2 ± 2.7	15.7 ± 2.6	14.4 ± 3.2	13.3 ± 3	9.234*	0.002*
Median (Min.–Max.)	17.5 (12–19)	16.5 (11–19)	13.5 (9–20)	13.5 (9–19)		
p_1		0.313	0.176	0.018*		
Botox ($n=10$)						
Mean ± SD	17.3 ± 1.8	15.9 ± 2.4	9.9 ± 3.6	10.9 ± 3.1	57.210*	< 0.001*
Median (Min.–Max.)	17.5 (15–20)	16 (12–20)	10 (6–16)	11 (7–15)		
p_1		0.016*	< 0.001*	< 0.001*		

SD: standard deviation

F: *F* test (ANOVA) with repeated measures, Sig. bet. periods was done using post hoc test (adjusted Bonferroni)

p: *p* value for comparing between the different studied periods

p_1: *p* value for comparing between PSQI 0 and each other period in each group

* Statistically significant at $p \leq 0.05$

to placebo, subcutaneous injections of Botulinum toxin A resulted in considerable alleviation of neuropathic pain after 24 weeks. Although this was in concordance with our study, this was subcutaneous not intradermal injection.

Hossam Egila and colleagues [16] injected 22 diabetic patients intradermally with Botulinum toxin A and compared to 20 patients on placebo. His study showed significant improvement of VAS 1, 4 and 12 weeks post-injection in patients injected with Botox in comparison

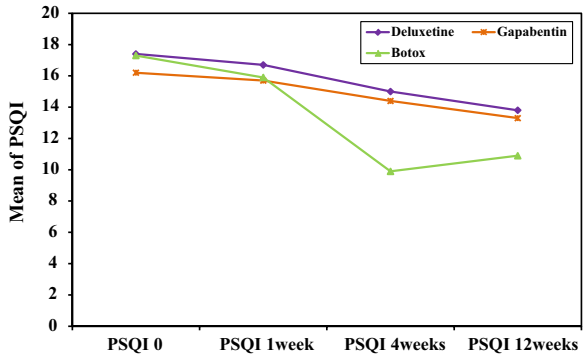

Fig. 2 Comparison between the different studied periods according to PSQI

to patients injected with placebo $p = (0.047, 0.001$ and $0.000)$, respectively. Yet there was no significant improvement in PSQI in patient injected with Botulinum toxin A.

Helmy and colleagues [17] in 2021 in Egypt also showed improvement of Overall Disability Sum Scale (ODSS) in 8 patients after intradermal injection of 8 units of Botulinum toxins type A in each foot in 6×4 distribution. Yet no significant change in the PSQ1 scale which was contrary to our results which showed that Botulinum type A intradermal decreased PSQ1 and this was statistically significant.

Also in a prospective, randomized, double-blind, controlled trial by Taheri and colleagues [18] in Iran on 141 patients, he compared Botulinum intradermal injection to placebo and reported significant improvement of VAS.

Conclusion

Botulinum toxin A injection had a comparable if not superior efficacy to duloxetine and gabapentin as a second-line treatment of diabetic peripheral neuropathy.

Abbreviations

VAS: Visual analogue score; Psq1: Pittsburgh Quality of Life Questionnaire 1; BTX-A: Botulinum neurotoxins; EC: Ethical committee; ICH GCP: International Conference of Harmonization Good Clinical practice; ODSS: Overall Disability Sum Scale.

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Author contributions

DEG: revision of the results and the manuscript and the corresponding author. HMD: idea of the research, follow-up of the participants, data collection and revision of the results. All authors read and approved the final manuscript.

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Availability of data and materials

The research data supporting the results reported in the article are totally available upon request from the authors.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee (EC) of Faculty of Medicine which is constituted and operates according to the International Conference on Harmonisation-Good Clinical Practice ICH GCP guidelines (Food and Drug Administration guideline) and applicable local and institutional regulations and guidelines which govern EC operation. The approval was obtained by the monthly meeting of EC on January 2021. And hence this research was registered in Alexandria faculty of medicine by number 2217 in February 2021.

Informed written consents from patients who participated in the study were obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Çakici N, Fakkel T, Van Neck J, Verhagen A, Coert J. Systematic review of treatments for diabetic peripheral neuropathy. Diabet Med. 2016;33(11):1466–76.
2. Rauck R, Makumi CW, Schwartz S, Graff O, Meno-Tetang G, Bell CF, et al. A randomized, controlled trial of gabapentin enacarbil in subjects with neuropathic pain associated with diabetic peripheral neuropathy. Pain Pract. 2013;13(6):485–96.
3. Weintraub MI, Wolfe GI, Barohn RA, Cole SP, Parry GJ, Hayat G, et al. Static magnetic field therapy for symptomatic diabetic neuropathy: a randomized, double-blind, placebo-controlled trial. Arch Phys Med Rehabil. 2003;84(5):736–46.
4. Valensi P, Le Devehat C, Richard J-L, Farez C, Khodabandehlou T, Rosenbloom RA, et al. A multicenter, double-blind, safety study of QR-333 for the treatment of symptomatic diabetic peripheral neuropathy: a preliminary report. J Diabetes Complicat. 2005;19(5):247–53.
5. Swislocki A, Orth M, Bales M, Weisshaupt J, West C, Edrington J, et al. A randomized clinical trial of the effectiveness of photon stimulation on pain, sensation, and quality of life in patients with diabetic peripheral neuropathy. J Pain Symptom Manage. 2010;39(1):88–99.
6. Campbell CM, Kipnes MS, Stouch BC, Brady KL, Kelly M, Schmidt WK, et al. Randomized control trial of topical clonidine for treatment of painful diabetic neuropathy. J Pain. 2012;153(9):1815–23.
7. Piovesan E, Teive H, Kowacs P, Della Coletta M, Werneck L, Silberstein S. An open study of botulinum-A toxin treatment of trigeminal neuralgia. Neurology. 2005;65(8):1306–8.
8. Argoff CE. A focused review on the use of botulinum toxins for neuropathic pain. Clin J Pain. 2002;18(6):S177–81.
9. Wang C, Zhang Q, Wang R, Xu L. Botulinum Toxin Type A for diabetic peripheral neuropathy pain: a systematic review and meta-analysis. J Pain Res. 2021;14:3855.
10. Yuan R-Y, Sheu J-J, Yu JM, Chen WT, Tseng I, Chang HH, et al. Botulinum toxin for diabetic neuropathic pain: a randomized double-blind crossover trial. Neurology. 2009;72(17):1473–8.
11. Ghasemi M, Ansari M, Basiri K, Shaigannejad V. The effects of intradermal botulinum toxin type a injections on pain symptoms of patients with diabetic neuropathy. J Res Med Sci. 2014;19(2):106.
12. Salehi H, Moussaei M, Kamiab Z, Vakilian A. The effects of botulinum toxin type A injection on pain symptoms, quality of life, and sleep quality of

patients with diabetic neuropathy: a randomized double-blind clinical trial. Iran J Neurol. 2019;18(3):99.
13. Taheri M, Sedaghat M, Solhpour A, Rostami P, Lima BS. The effect of Intradermal Botulinum Toxin a injections on painful diabetic polyneuropathy. Diabetes Metab Syndr. 2020;14(6):1823–8.
14. Moon YE, Choi JH, Park HJ, Park JH, Kim JH. Ultrasound-guided nerve block with botulinum toxin type A for intractable neuropathic pain. Toxins. 2016;8(1):18.
15. Eitner L, Vollert J, Maier C, Attal N. Botulinumtoxin-A-Injektionen bei neuropathischem Schmerz. Der Schmerz. 2017;31(5):524–6.
16. Hossam Egila HE, Gomaa M, Abdel-naby A, Shehab El-din M. Botulinum toxin type A in severe diabetic neuropathy. Benha Med J. 2020;37:723–30.
17. Helmy S, Emara T, Menem AA. Botulinum toxin type A for painful diabetic neuropathy: an open-label study. Egypt J Neurol Psychiatr Neurosurg. 2021;57(1):1–3.
18. Taheri M, Sedaghat M, Solhpour A, Rostami P, Lima BS. The effect of Intradermal Botulinum Toxin a injections on painful diabetic polyneuropathy. Diabetes Metab Syndr Clin Res Rev. 2020;14(6):1823–8.

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