Comparison between Utilization of Botox Versus Fluticasone Furoate in Patients with Intermittent Allergic Rhinitis: A Randomized, Controlled Trial

Diaa El Din Mohamed El Hennawi and Mohamed Rifaat Ahmed*

Otolaryngology Unit, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Abstract: *Background*: Allergic rhinitis is a common disease affects about 5 to 22% from general population. Botulinum toxin is a neurotoxic protein assumed to lead to symptomatic control of intermittent allergic rhinitis**.**

Objectives: To compare between utilization of botulinum toxin type A versus fluticasone furoate in treatment of intermittent allergic rhinitis.

Patients and Methods: A randomized clinical controlled trial study created on seventy two adult patients with intermittent allergic rhinitis divided into two groups**;** Group B (BTX-A) and Group F (fluticasone furoate).

Results: After one month the mean intensity of nasal symptoms according to VAS among the Group B (BTX-A) sneezing was 2.41 while 2.16 in Group F (fluticasone furoate). The difference is not statistically significant.

Conclusions: Intranasal injection of Botulinum A(BTX-A) is a highly effective, safe, and simple procedure, with a long-lasting symptomatic relief for patients with intermittent allergic rhinitis. It as a might be used as an alternative treatment for fluticasone furoate nasal spray.

Keywords: Rhinitis, Allergic, Botox, Fluticasone.

INTRODUCTION

Allergic rhinitis is very common disease affects about 5-22% from world population with about 9% of all visits to physicians for the allergic diseases [1].

Symptoms of allergic rhinitis may include congestion, rhinorrhea, postnasal drip, sneezing, itchy nose and watery eyes [2]. Physical findings may support the diagnosis as nasal mucosa tends to be pale, bluish, congested and covered by copious watery discharge [3].

Botulinum toxin is a neurotoxic protein produced by the bacterium Clostridium botulinum. It is one of the most poisonous naturally occurring substances in the world [4].

By 1973, Alan B Scott, used botulinum toxin type A (BTX-A) in monkey experiments, and, in 1980, he officially used BTX-A for the first time in humans to treat strabismus. In December 1989, BTX-A was approved by the US Food and Drug Administration (FDA) for the treatment of strabismus, blepharospasm, and hemi facial spasm in patients over 12 years old [4].

BTX-A acts by inhibiting acetylcholine release, thus interferes with nerve impulses and causes paralysis of muscles in botulism [5].

Unal *et al.*, mentioned that injection of 40 units of BTX-A into the turbinate, as a single agent, may help the symptomatic control of allergic rhinitis up to 8 weeks [6].

Cengiz *et al.* also mentioned that intranasal injection of BTX-A is a highly effective, safe, and simple symptomatic treatment with a long-lasting effect for patients with intrinsic rhinitis [7].

Fluticasone furoate is a synthetic corticosteroid derived from fluticasone, used for treating common nasal allergy symptoms, such as itching, sneezing, and runny or stuffy nose [8].

Specific effects of fluticasone furoate demonstrated in activation of the glucocorticoid response element, inhibition of pro-inflammatory transcription factors such as NFkB, and inhibition of antigen-induced lung eosinophilia in sensitized rats [9].

Fluticasone furoate has been shown *in vitro* to exhibit a binding affinity for the human glucocorticoid receptor that is approximately 29.9 times that of dexamethasone and 1.7 times that of fluticasone propionate [10-11].

The aim of this study was to compare the efficacy of botulinum toxin type A (BTX-A) versus fluticasone furoate in patients with intermittent allergic rhinitis

*Address correspondence to this author at the Otolaryngology Unit, Faculty of Medicine, Suez Canal University, Ismailia, Egypt; Tel: +20185043825;
Fax: +20663415603; E-mail: m_rifaat@hotmail.com

E-ISSN: 2308-7978/15

MATERIALS AND METHODS

A randomized clinical controlled trial study was conducted in the otolaryngology department – Suez canal university – Ismailia – Egypt from June 2007 to April 2011. The study protocol was approved by the ethical committee of faculty of Medicine. A written consent was obtained from all patients.

Seventy two adult patients attended to the outpatient clinic with the intermittent allergic rhinitis (less than 4 days a week or 4 weeks a year) and positive skin test were included. The presenting symptoms were nasal obstruction, watery rhinorrhea, postnasal drip, sneezing, itchy nose and redness of eyes) [2].

Exclusion criteria comprised true hypertrophy of the inferior turbinate, chronic rhino sinusitis, nasal polyposis, antrochoanal polyps, deviated septum, smoking, pregnancy, negative skin test and any previous nasal surgery.

All patients were required to complete a questionnaire assessing their nasal symptoms, pre-treatment and one month after treatment. In all patients, a visual analogue scale (VAS) was used to assess subjective symptoms, with 0 indicating no symptoms and 10 indicating severe and/or constant symptoms. Anterior rhinoscopy, nasal endoscopic and computed tomography of nose and paranasal sinuses were performed to all patients.

Aspiration of the nasal secretions from the inferior meatus, then immediately fixed in 95% alcohol and interacted with the appropriate stain before treatment.

The patients were randomly divided into two groups in the following manner:. opaque envelopes were numbered sequentially from1 to 40. A computer-generated table of random numbers was used for treatment assignment: if the last digit of the random number was from 0 to 4, a note was placed into the envelope specifying intra nasal Botox while if the last digit was from 5 to 9 the note specified Fluticasone furoate nasal spray. The envelopes were sealed. As eligible participants were entered into the trial, the envelopes were opened in sequential order to give each patient his or her randomized group assignment.

Group B (BTX-A group), 20 units of BTX-A was injected (total 40 units) into middle and inferior turbinate under surface anesthesia using zero endoscope [7].

Group F(fluticasone furoate group) two sprays in each nostril once daily for topical administration to the nasal mucosa by means of a metering (50 µL) for one month [12].

All of the patients were examined after one month for for nasal allergic symptoms and any side effects could be happened.

Statistical Analysis

Data which were collected from the patients' symptoms for both groups (B&F) before and after one month were entered to soft ware SPSS.

p value was obtained where was significant if P<0.5.T student test was done to evaluate the significance of BTX-A injection on reliving the symptoms versus fluticasone furoate nasal spray.

Ethical Considerations

Written consent was obtained from all patients. The local ethics committee approved the study.

RESULTS

In the present study 72 patients with intermittent allergic rhinitis (with mean age 25.4 years) were included. Patients were randomly divided into 2 groups: Group B: 36 patients, 24 females & 12 males While Group F: 36 patients, 27 females & 9 males.

All the patients in both groups had positive skin prickle test with positive allergic nasal smear condition ratio of approximately goblet to columnar cells of 4:1.

The main presenting symptoms were: sneezing in 31 patients (86, 1%) in group B while it was in 30 patients (83.3%) in Group F, followed by itchy nose in 27 patients (75%) in group B and 26 patients (72.2%) in group F, nasal obstruction in 24 patients (66.6) in group B and 25 patients (69.4%) in group F, red eyes in 20 patients (55.5%) in group B and 21patients (58.3%)in group F and watery rhinorrhea in 19 patients (52.7%) in group B and in 18 patients (50%) in group F. while post nasal discharge was the least presenting symptom found in only 8 patients (22.2%) in both groups. As regard the presenting symptoms there was no statistically significance difference between both groups Table **1**.

The main nasal findings among the patients were: pale, bluish mucosa in 29 (80. 5%) in group B while in 30 patients (83.3%) in Group F, watery mucosa in 20

Table 1: Shows the Symptoms Among both Group B (BTX-A) and Group F (Fluticasone Furoate)

Symptoms	Group B (BTX-A)		Group F (fluticasone furoate)		P value
	N = (36)	%	N = (36)	%	
Nasal obstruction,	24	66.6	25	69.4	0.21
watery rhinorrhea	19	52.7	18	50	0.13
sneezing	31	86.1	30	83.3	0.89
itchy nose	27	75	26	72.2	0.57
red eyes	20	55.5	21	58.3	0.48
Post-nasal drip	8	22.2	8	22.2	0.21

N = number of patients.
Insignificant p>0.05.

Table 2: Shows the Nasal Examination Findings among both Group B (BTX-A) and Group F (Fluticasone Furoate)

Nasal examination findings	Group B (BTX-A)		Group F (fluticasone furoate)		P
	N = (36)	%	N = (36)	%	
pale, bluish mucosa	29	80.5	30	83.3	0.73
Watery mucosa	20	55.5	19	52.7	0.43
Infra orbital edema	17	47.2	18	50	0.18
Allergic shiner	5	13,8	6	16.6	0.79

N = number of patients.
Insignificant p>0.05.

patients (55.5%) in group B and 19 patients (52.7%) in group F, infra orbital edema in 17 patients (47.2%) in group B and 18 patients (50%) in group F. and allergic shiner in 5 patients (13,8%) in group B and in 6 patients (16,6 %) in group F. There were no statistically significant difference between both groups Table **2**.

The mean intensity of nasal symptoms according to VAS before treatment among both groups were demonstrated in Table **3**. There was no statistically significant difference between both groups.

After one month the mean intensity of nasal symptoms according to VAS among both groups were shown in Table **4** and Figure **3** with no statistically significant difference between both groups.

There was marked improvement in mean intensity of nasal symptoms according to VAS in both as seen in Figures **2** & **3**. No side effects were reported from both drugs.

DISCUSSION

Allergic rhinitis, the most common atopic diseases, is an important public health problem as it affects up to 20% of the adult population in world [13].

Table 3: Shows the Mean Intensity Symptoms among Group B and Group F before Treatment

Symptom VAS Before TTT	Group B (BTX-A)		Group F (fluticasone furoate)		P
	Mean	SD	Mean	SD	
Congestion and obstruction,	6.17	0.76	6.83	0.91	0.314
watery rhinorrhea	6.68	1.23	6.16	0.96	0.14
sneezing	7.76	0.92	7.03	1.28	0.25
itchy nose	5.32	0.59	5.91	1.02	0.59
red eyes	4.92	1.86	4.69	0.94	0.215
Post-nasal drip	2.11	1.18	2.38	1.06	0.49

Insignificant p>0.05.

Table 4: Shows the Mean Intensity Symptoms among group B and Group F after One Month

Symptom VAS After one month	Group B (BTX-A)		Group F (fluticasone furoate)		P
	Mean	SD	Mean	SD	
Congestion and obstruction,	1.02	0.96	1.11	0.86	0.26
watery rhinorrhea	1.96	0.38	1.83	0.46	0.22
sneezing	2.41	1.02	2.16	1.12	0.18
itchy nose	1.36	0.56	1.12	0.83	0.39
watery eyes	1.01	0.81	1.16	0.93	0.17
Post-nasal drip	1.12	0.11	1.09	0.26	0.31

Insignificant p>0.05.

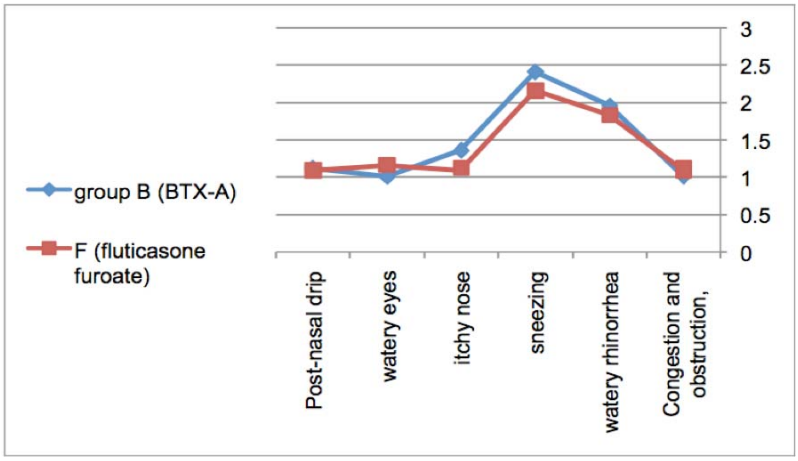

Figure 1: Shows the mean intensity symptoms among group B (BTX-A) and Group F (fluticasone furoate) after one month.

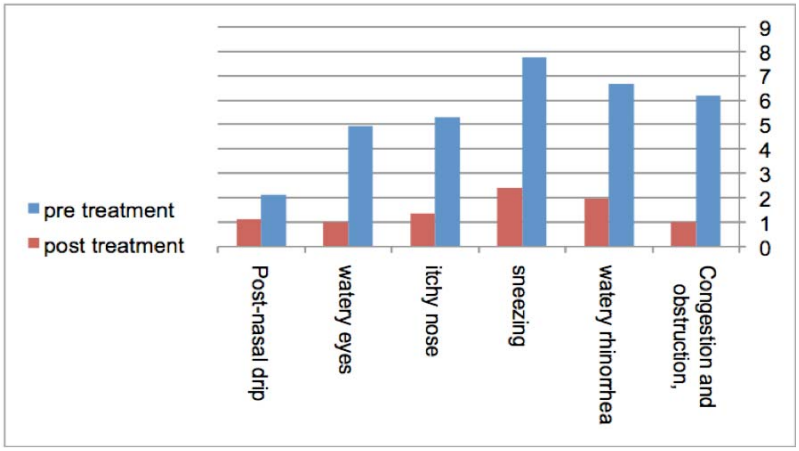

Figure 2: Shows the mean intensity symptoms among group B (BTX-A) pre & post treatment.

In addition, it is the sixth most prevalent chronic condition in the world, and its prevalence is increasing in the last decades [14].

Quality-of-life studies demonstrate that allergic rhinitis causes significant impairment of function, exceeding that of heart disease and asthma [15-16].

Based on Unal *et al.* 2004 who find that there was no significant difference between 20 and 30 units of BTX-A injection in his study groups, so in the present study we used the 20 units as a lower effective dose

After one month we found that all of the symptoms were significantly improved in both groups Tables **3**, **4**.

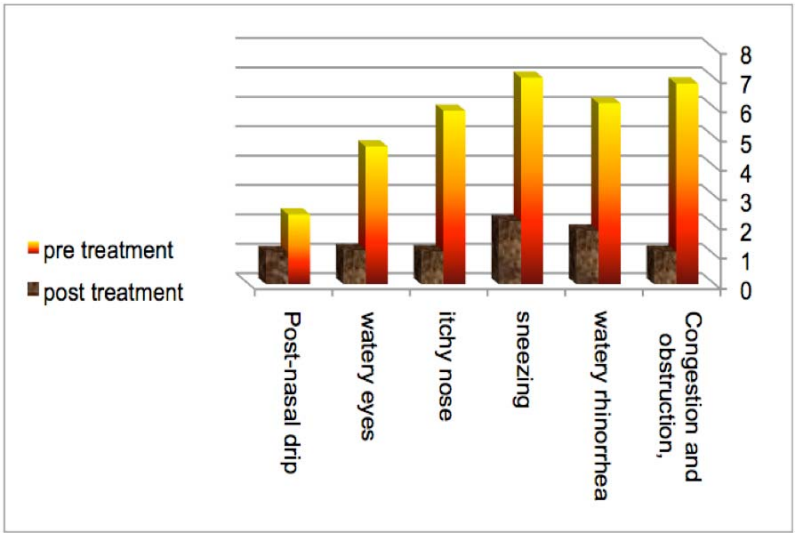

Figure 3: Shows the mean intensity symptoms among group F (fluticasone furoate) pre & post treatment.

This was similar to the findings of Unal *et al.* 2004 who found that rhinorrhea, nasal, obstruction and sneezing scores in injected group with BTX-A were significantly better than those in Control Group [6].

On the other hand, Cengiz and Ozcan used only 10 units of BTX-A intranasal they found that total symptom scores only decreased and there was delay of improvement up to one month [7-17].

Schleimer, 1993 mentioned that topical intranasal glucocorticosteroids are potent medications for the treatment of allergic rhinitis. These agents profoundly reduce multiple aspects of the inflammatory response to allergen [18].

Comparison between improvements in patients symptoms in both groups: shows no statically significant difference after one month.

Brin *et al.* 1999 mentioned that the type A toxin proteolytically degrades the SNAP-25 protein, a type of SNARE protein. The SNAP-25 protein is required for the release of neurotransmitters from the axon endings [4].

While treatment with intranasal flunisolide resulted in significant inhibition of mediator release during both early- and late-phase reactions after antigen challenge, along with a significant inhibition of the influx of basophils, eosinophils, neutrophils, and mononuclear cells in nasal secretions and the priming response to antigen [19-21].

Both drugs are not in challenge but they are complementary and are different weapons with physician. As botox is preferred in patients with poor compliance as it is considered simple, safe and applied once.

CONCLUSION

Intranasal injection of BTX-A is a highly effective, safe, and simple procedure with a long-lasting effect for patients with intermittent allergic rhinitis. It is as a good as fluticasone furoate nasal spray in controlling nasal symptoms.

SUMMARY

- Allergic respiratory disease is very common disease varies from 5-22%.
- Botulinum toxin is a neurotoxic protein may help the symptomatic control of allergic rhinitis**.**
- The study was carried out to compare between efficacies of botulinum toxin type A versus fluticasone furoate in patients with intermittent allergic rhinitis.
- Intranasal injection of BTX-A is a highly effective, safe, and a good alternative treatment as fluticasone furoate nasal spray in treatment allergic rhinitis.

REFERANCES

[1] Holm A, Fokkens W. Topical Corticosteroids in Allergic Rhinitis; effects on nasal inflammatory cells and nasal mucosa. Laryngosc 2001; 31(4): 529-35.

[2] Ratner P, Ehrlich P, Fineman S. Use of Intranasal Cromolyn Sodium for Allergic Rhinitis. Mayo Clin Proceed 2002; 77(4): 350-4.
http://dx.doi.org/10.4065/77.4.350

[3] Nathan R. Pharmocotherapy for Allergic Rhinitis: a Critical Review of Leukotriene Receptor Antagonists Compared with other Treatments. Ann of Aller Asth Immuno 2003; 90: 182-91. http://dx.doi.org/10.1016/S1081-1206(10)62138-2

[4] Brin MF, Lew MF, Adler CH, *et al*. Safety and efficacy of NeuroBloc (botulinum toxin type B) in type A-resistant cervical dystonia. Neurology 1999; 53 (7): 1431-8. http://dx.doi.org/10.1212/WNL.53.7.1431

[5] Hill EV. Botulism. In: Summary Report on B. W. Investigations. Memorandum to Alden C. Waitt, Chief Chemical Corps, United States Army, December 12, 1947; tab D. Archived at the US Library of Congress.

[6] Unal M, Sevim S, Dogu O, Vayisoglu Y, Kanik A. Effect of botulinum toxin type A on nasal symptoms in patients with allergic rhinitis: a double-blind, placebo-controlled clinical trial. Acta Otolaryngol 2004; 124(10): 1240.

[7] Ozcan C, Vayisoglu Y, Doğu O, Görür K. The effect of intranasal injection of botulinum toxin A on the symptoms of vasomotor rhinitis. Asian Pac J Allergy Immunol 2006; 24: 17-25.

[8] Bruni FM, De Luca G, Venturoli V, Boner AL. Intranasal corticosteroids and adrenal suppression. Neuroimmunomodulation 16(5): 353-62.

[9] Martin BG, Ratner PH, Hampel FC, *et al*. Optimal dose selection of fluticasone furoate nasal spray for the treatment of seasonal allergic rhinitis in adults and adolescents. Allergy and asthma proceedings: the official journal of regional and state allergy societies 2007; 28(2): 216-25. http://dx.doi.org/10.2500/aap.2007.28.2983

[10] Kaiser HB, Naclerio RM, Given J, Toler TN, Ellsworth A, Philpot EE. Fluticasone furoate nasal spray: A single treatment option for the symptoms of seasonal allergic rhinitis. J Allergy Clin Immunol 2007; 119(6): 1430-7. http://dx.doi.org/10.1016/j.jaci.2007.02.022

[11] Mamikoglu B, Houser S, Corey J. An Interpretation Method of Objective Assessment of Nasal Congestion with Acoustic Rhinometry. Laryngoscope 2002; 112(5): 926-29. http://dx.doi.org/10.1097/00005537-200205000-00027

[12] Harold BK, Robert MN, John G, Tom NT, Anna E. Fluticasone furoate nasal spray: A single treatment option for the symptoms of seasonal allergic rhinitis. J Aller Clin Immunol 2007; 119(6): 1430-7. http://dx.doi.org/10.1016/j.jaci.2007.02.022

[13] Sly RM. Changing prevalence of allergic rhinitis and asthma. Ann Allergy Asthma Immunol 1999; 82: 233-48. http://dx.doi.org/10.1016/S1081-1206(10)62603-8

[14] Collins J, Ed. Prevalence of selected chronic conditions, United States, 1983–1985. Hyattsville (MD): US Public Health Service. Advance data from Vital and Health Statistics, No 155. Vol DHHS Pub No (PHS): 88.

[15] Juniper EF, Guyatt GH. Developing and testing a new measure of health status for clinical trials in rhinoconjunctivitis. Clin Exp Allergy 1991; 21: 77-83. http://dx.doi.org/10.1111/j.1365-2222.1991.tb00807.x

[16] Juniper EF, Guyatt GH, Anderson B, *et al*. Comparison of power and aerosolized budesonide in perennial rhinitis: validation of rhinitis quality of life questionnaire. Ann Allergy 1993; 70: 225-30.

[17] Ozcan C, Vayisoglu Y, Dogu O, Gorur K. The effect of intranasal injection of botulinum toxin A on the symptoms of vasomotor rhinitis: Am J Otolaryngol 2006; 27(5): 314-8. http://dx.doi.org/10.1016/j.amjoto.2006.01.008

[18] Schleimer R. Glucocorticosteroids: their mechanisms of activation and use in allergic diseases. In: Middleton EJ, Reed CE, Ellis EF, *et al*, editors. Allergy: principles and practice. 4th ed. St. Louis: Mosby-Year Book; 1993; pp. 893–925.

[19] Pipkorn U, Proud D, Lichtenstein LM, *et al*. Inhibition of mediator release in allergic rhinitis by pre- treatment with topical glucocorticosteroids. N Engl J Med 1987; 316: 1506-10. http://dx.doi.org/10.1056/NEJM198706113162403

[20] Bascom R, Wachs M, Naclerio RM, *et al*. Basophil influx occurs after nasal antigen challenge: effects of topical corticosteroid pretreatment. J Allergy Clin Immunol 1988; 81: 580-9. http://dx.doi.org/10.1016/0091-6749(88)90198-4

[21] Bascom R, Wachs M, Naclerio RMl. Basophil influx occurs after nasal antigen challenge: effects of topical corticosteroid pretreatment. J Allergy Clin Immunol 1988; 81: 580-9. http://dx.doi.org/10.1016/0091-6749(88)90198-4

Received on 24-01-2015 Accepted on 04-03-2015 Published on 10-03-2015

DOI: http://dx.doi.org/10.12970/2308-7978.2015.03.01.5