

Comparative Efficacy of H₁ blocker, H₂ blocker, and Corticosteroid Individually and in Combination in Resolution of Sign and Symptoms of Acute Urticaria

1. Ashfaq Ahmad Shah Bukhari 2. Ghulam Nabi Khokhar 3. Ghulam Rehmani Lakho
4. Mohsin Shah

1. Asstt. Prof. of Physiology, Rehman Medical College (RMC), Peshawar 2. Prof. of Pharmacology, RMC, Peshawar 3. Professor of Physiology, RMC, Peshawar 4. Asstt. Prof. of Physiology, IBMS Peshawar.

ABSTRACT

Objective: To compare the efficacy of H₁ blocker, H₂ blocker, corticosteroid in combination or individually in resolution of the sign and symptoms of acute urticaria.

Study Design: Randomized control trial

Place and Duration of Study: This study was carried out at Medical Department, Naseer Teaching Hospital, Peshawar, Khyber Pakhtunkhwa (KPK) for the period of six months (July 2012 through December 2012).

Materials and Methods: In this study 140 adult patients of both gender with acute urticaria were treated with either H₁ blocker (group A), H₂ blocker (group B) or in combinations of H₁ blocker + H₂ blocker (group C), H₁ blocker + H₂ blocker + dexamethasone (group D), H₁ blocker + dexamethasone (Group E), H₂ blocker + dexamethasone (Group F) or Dexamethasone (group G) alone. The end points were resolution of sign and symptoms in each group of patients (minimum 3 hours after treatment). Pregnant females, anemic and Patients with cardiac disease were excluded.

Results: H₁+ H₂ blockers + dexamethasone found to be most effective therapeutic combination (95% of patients) in resolution of sign and symptoms of acute urticaria, followed by H₁ blocker + dexamethasone (90%) and H₁+ H₂ blockers (85%).

Conclusion: This study concludes that the combination of H₁+H₂ blockers + dexamethasone is more effective in relieving the patient from the sign and symptom of acute urticaria as compared to H₁ blocker or H₂ blocker or dexamethasone given alone or in combination of any two.

Key Words: Urticaria, H₁ blocker, H₂ blocker, dexamethasone

INTRODUCTION

Urticaria is commonly referred to as hives, is the most frequent dermatologic disorder seen in the Emergency Department (ED). It appears as raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis that are very pruritic¹⁻². It is characterized by typical lesion or wheal formation which is often erythematous, usually pruritic papule or plaque that appears and disappears over relatively short periods of time³. They are caused by vasoactive mediators, predominantly histamine, released from mast cells. In the vast majority of cases the wheal is transient, lasting for only a few hours in any one place, but with new wheal appearing in other places⁴.

Urticaria is one of the most common dermatologic problems and 20-30% of individuals have at least one attack of urticaria in their lifetime⁵⁻⁶. Both children and adults may develop urticaria with the peak age of onset in adults being between 20 and 40 years of age⁴. Urticaria may be acute when the duration is less than 6 weeks⁷ or chronic when it lasts for more than 6 weeks^{5,8}. Acute urticaria usually develops more severe

clinical and life-threatening symptoms compared with chronic urticaria⁹⁻¹⁰. Common causes of urticaria are drugs, infections, parasites, food and food colours, systemic disease, psychogenic factors, autoimmune disease, endocrine disease and malignancy³. Acute urticaria is more common and is characterized with more severe symptoms at onset, which may be life threatening. Clinical symptoms of chronic urticaria are often less severe but much more troublesome than those of acute urticaria, chronic urticaria may have highly variable etiological factors and duration¹¹. Large variety of urticaria variants exist, including acute immunoglobulin-E (IgE) mediated urticaria, chemical-induced urticaria, autoimmune urticaria, delayed pressure urticaria, cholinergic urticaria, cold urticaria, solar urticaria, aquagenic urticaria, physical urticaria and many others¹⁻².

Urticaria may be often confused with a variety of other dermatologic diseases that are similar in appearance and are pruritic including maculopapular drug eruption, atopic dermatitis (eczema), contact dermatitis, erythema multiform, insect bites, pityriasis rosea and others.

Usually, the experienced clinician is able to distinguish these from urticaria because of its distinctive appearance, the fact that it is intensely pruritic, and because it blanches completely with pressure¹².

A number of studies showed the effectiveness of antihistamines treatment either with H₁ blocker¹³⁻¹⁵ or with H₂ blocker¹⁶ or their combination in treatment of acute urticaria¹⁷ but these remained ineffective in the treatment or prevention of most forms of urticaria. In addition corticosteroid therapy involving a multitude of formulation is widely used in nearly all fields of medicine¹⁸. Although the combination of H₁ blocker and H₂ blocker has been reported to improve certain cutaneous outcomes in patients with acute allergic syndromes¹⁶, data is scanty on combination therapy of acute urticaria. However to the best of our knowledge the data on combination of H₁ blocker + H₂ blocker with dexamethasone is lacking.

MATERIALS AND METHODS

A total of 140 patients with urticaria were treated with mentioned drugs alone or in combination who presented at out-patient department of Medical Department, Naseer Teaching Hospital, Peshawar during six months (from July 2012- December 2012). Patients between ages 20-60 years of both gender were included in this study who visited the hospital with urticaria developed due to any reason e.g. history of drug intake, history of disease, history of food intake and any allergic reaction which induced urticaria. Approval of hospital ethical committee and informed written consent were taken from the subject. Pregnant ladies and patients with anemia, heart diseases or any other illness were excluded.

Proper history was taken from all the patients. Diagnosis was made on basis of clinical presentation, physical examination and pathological findings. Patients were divided in seven equal groups; A (treated with 22.7mg H₁ blocker), B (treated with 50mg H₂ blocker), C (treated with 22.7mg H₁ blocker + 50mg H₂ blocker), D (treated with 22.7mg H₁ blocker + 50mg H₂ blocker + 4mg Dexamethasone), E (treated with 22.7mg H₁ blocker + 4mg Dexamethasone), F (treated with 50mg H₂ blocker + 4mg Dexamethasone) and G (treated with 4mg dexamethasone). Each group comprises of 20 patients. Patients were observed for minimum of three hours after treatment to evaluate and compare the efficacy of drugs in each group. Duration of the effectiveness was also measured to see the interval of effective drug. All the data collected in pre designed proforma and recorded on SPSS 10.

RESULTS

As depicted in table-1 males were 78 (56%) with 62 (44%) female. Known etiological findings of acute urticaria in clinical history taking revealed six patients (4%) with positive history of either respiratory tract

infection, gastrointestinal infection, whereas fifteen patients (11%) had positive history of drug intake i.e. ciprofloxacin, metronidazole, non-steroidal anti-inflammatory drugs. Four patients (3%) had positive history of food induced acute urticaria i.e. fish, nuts and mushroom as shown in table 2.

Table No.1: Frequency and percentage with relation to different ages.

	Frequency (s)	Percentage
Age		
20-30 years	51	36%
30-40 years	53	38%
40-50 years	27	20%
50-60 years	09	06%
Male	78	56%
Female	62	44%
Total	140	

Table No.2: History of finding of subjects.

History findings	Response	Frequency (s)	Percentage
History of Disease	Yes	6	4%
	No	134	96%
History of drug intake	Yes	15	11%
	No	125	89%
History of food intake	Yes	4	3%
	No	136	97%
Total		140	

Table No.3: Efficacy of drugs in different groups of subjects.

Groups	Effectiveness	Efficacy Frequency (n)	Percentage	Total
H ₁ Blocker	Effective	14	70%	20 cases
	Not Effective	6	30%	
H ₂ Blocker	Effective	5	25%	20 cases
	Not Effective	15	75%	
H ₁ +H ₂	Effective	17		
	Not Effective	3		
H ₁ +H ₂ + dexamata- sone	Effective	19	85%	20 cases
	Not Effective	1	15%	
H ₁ + dexamata- sone	Effective	18	90%	20 cases
	Not Effective	2	10%	
H ₂ + dexamata- sone	Effective	11	55%	20 cases
	Not Effective	9	45%	
dexamata- sone	Effective	8	40%	20 cases
	Not Effective	12	60%	

Table-3 depicted the most effective treatment in the resolution of sign and symptoms. H₁ blocker + H₂ blocker with dexamethasone were effective in 95% whereas rest of the combination of treatment or individual treatment showed less therapeutic efficacy. Table-4 showed effectiveness of the treatment i.e. how quickly drug resolves the symptoms of urticaria after

drug treatment (minimum 3 hours). Fastest resolution of symptoms occurs in group of patients treated with H₁ blocker + H₂ blocker with dexamethasone (between 15-40 minutes). Whereas longest duration was observed in patients treated with H₂ blocker (3-6 hours).

Table No.4: Duration of effectiveness of drugs in subjects

Groups	Duration of Effectiveness
H ₁ Blocker	2-4 hours
H ₂ Blocker	3-6 hours
H ₁ +H ₂	1-2 hours
H ₁ +H ₂ + dexamatasone	15-40 minutes
H ₁ + dexamatasone	1 hour
H ₂ + dexamatasone	2 hours
dexamatasone	2 ½ hours

DISCUSSION

Antihistamines are widely used group of drugs for the treatment of acute urticaria. A number of studies showed the effectiveness of antihistamines treatment either with H₁ blocker¹³⁻¹⁵ or with H₂ blocker¹⁶ or their combination in treatment of acute urticaria¹⁷. Linet *al* showed pretreatment effect for H₂ blocker in allergic reaction. Their study demonstrates the benefit of adding H₂ blocker to H₁ blocker antihistamine in treatment of ongoing allergic reactions¹⁶. Although few studies described the effects of both H₁ and H₂ blockers in treatment of acute urticaria¹⁶, our study has the value of evaluating different combinations of H₁ blocker, H₂ blocker and corticosteroid. The maximum efficacy in our study was observed in patients received the combination of H₁ blocker + H₂ blocker with dexamethasone (95%) followed by the combination of H₁ blocker + dexamethasone which was effective in 90% cases and the combination of H₁ blocker + H₂ blocker was effective in 85% cases. On the other hand effectiveness of H₁ blocker was found in 70%, H₂ blocker was found in 25% while dexamethasone was found in 40% cases as shown in table-3. Similar observation has been reported by Zuberbier *et al* had mentioned that combination therapy with H₁ and H₂ histamine blockers can benefit patients with acute allergic syndromes¹⁹. Similar observations were also recorded by Lin *et al* that most cases of simple acute urticaria can be treated with H₁ antihistamine agents. In cases of severe or persistent urticaria, H₂ antihistamines may be added and are probably additive to the effect of H₁ antihistamines if simultaneously given intravenously¹⁶.

Some patients with urticaria had only cutaneous symptoms whereas some patients had systemic symptoms such as headache, joint pain and gastrointestinal complaints as well⁹⁻¹⁰. Results of the present study showed that the number of patients was more with the history of drug induced urticaria 11% as

compared to the history of food intake induced urticaria patients which were 3% and history of disease induced urticaria patients which were 4%. In this study, most commonly reported drugs which induced urticaria were ciprofloxacin, metronidazole, aspirin, and non-steroidal anti-inflammatory drugs. Urticaria induced by food was due to intake of fish, nuts and mushroom. Diseases which cause urticaria include respiratory tract infections²⁰. Similarly, it was observed that 4% urticaria patients in this study had a history of these diseases.

Another merit of our study is the assessment of degree of effectiveness of the drug in all groups in terms of duration of time in which drug showed its effect to clearly resolve the symptoms of urticaria. The patients were observed for a minimum of 3 hour in the current study. Results of the present study showed that combination of H₁ + H₂ blockers and dexamethasone took lesser time in effectiveness as compared to H₁ or H₂ blockers and dexamethasone alone. The results also revealed that the duration of effectiveness of H₁ blocker + H₂ blocker + dexamethasone was observed between 15-40 minutes followed by H₁ blocker + H₂ blocker in which the duration of effectiveness was 1-2 hours and duration of effectiveness of H₁ + dexamethasone was only one hour. On the other hand duration of effectiveness of H₁ blocker was 2-4 hours, H₂ blocker was 3-6 hours and dexamethasone effectiveness was found to be 2 ½ hours as shown in table-4. An improved outcome over the course of one or two hours was seen with combined H₁ blocker and H₂ blocker in patients who were presented with urticaria and angioedema¹⁶. However, in this study no such significant difference of H₁ blocker, H₂ blocker and dexamethasone was found in different age group and in gender distribution.

No patients developed any severity to intubate or resuscitate them. Parenteral route of administration was used for the patients in all age groups of the present study. No trials of treating the patients orally were done in this study, the medication and treatment resulted in rapid improvement in signs and symptoms of urticaria. However, further studies and trials are needed to ascertain whether similar results are observed if the drugs are administered orally in different age groups of patients suffering from urticaria. The small number of sample size in each group may be the limitation of this study.

CONCLUSION

Patients presented with acute urticaria in all groups did not have any specific difference regarding gender and age. The statistical difference is noted in improvement of urticaria with different drugs treatment and duration of resolution of signs and symptoms. The presentation of patients was almost same but was treated with different drugs and different strategies. The poorest response was noted with H₂ blocker alone and while

treatment with H₁blocker + H₂blocker + dexamethasone gave excellent response in acute urticaria as compared to H₁blocker alone, H₁ + H₂blockers and dexamethasone alone.

REFERENCES

1. Najib U, Sheikh J. An update on acute and chronic urticaria for the primary care provider. *Postgrad Med* 2009;121: 141-151.
2. Poonawalla T, Kelly B. Urticaria : a review. *Am J Clin Dermatol* 2009;10: 9-21.
3. Altunay IK, Demirci GT, Atis G. Clinical Observations on Acute and Chronic Urticaria: A comparative Study. *J Clin Exp Dermatol Res* 2011; 2:7.
4. Deacock SJ. An approach to the patient with urticaria. *Clin and Exp Immunol* 2008;153: 151-161.
5. Khalaf AT, Li W, Jinquan T. Current advances in the management of urticaria. *Arch Immunol Ther Exp* 2008; 56: 103-114.
6. Maurer M, Grabbe J. Urticaria: Its History-Based Diagnosis and etiologically oriented treatment. *Dtsch Arztebl Int* 2008; 105:458-66.
7. Habif TP. *Clinical dermatology: a color guide to diagnosis and therapy*. 4th ed. Chile: Mosby; 2004.
8. Zuberbier T, Maurer M. Urticaria: Current opinions about etiology, diagnosis and therapy. *Acta Derm Venereol* 2007;87:195-205.
9. Arshod SH, Holgate ST, Adkinson NF, Babu KS. *An Atlas of Investigation and Management Allergy*. Oxford, Atlas Medical Publishing Ltd 2005.
10. Ferrer M. Epidemiology, healthcare resources, use and clinical features of different type of urticaria. *J Investing Allergol Clin Immunol* 2009;19: 21-26.
11. Maurer M, Ortonne P, Zuberbier T. Chronic urticaria: an internet survey of health behaviors, symptom patterns and treatment needs in European adult patients. *Br J Dermatol* 2009;160: 633-641.
12. Frigas E, Park MA. Acute urticaria and angioedema: diagnostic and treatment considerations. *Am J Clin Dermatol* 2009;10: 239-250.
13. Wanderer AA, Bernstein IL, Goodman DL. The diagnosis and management of urticaria: a practice parameter. *Acute urticaria/angioedema*. *Ann Allergy Asthma Immunol* 2000; 85: 525-531.
14. Simons FER. Prevention of acute urticaria in young children with atopic dermatitis. *J Allergy Clin Immunol* 2001;107: 703-6.
15. Kobza BA, Lawlor F, Greaves MW. Consensus meeting on the definition of physical urticarias and urticarial vasculitis. *Clin Exp Dermatol* 1996;21: 424-6.
16. Lin RY, et al. Improved outcomes in patients with acute allergic syndromes who treated with combined H₁ and H₂ antagonists. *Ann Emerg Med* 2000;36: 462-468.
17. Kaliner M, Sigler R, Summers R. Effects of infused histamine: analysis of the effects of H-1 and H-2 histamine receptor antagonists on cardiovascular and pulmonary responses. *J Allergy Clin Immunol* 1981;68: 365-371 .
18. Williams P, Sewell WAC, Bunn C, Pumphrey R, Read G, Jones S. *Clinical Immunology Review Series: an approach to the use of the immunology laboratory in the diagnosis of clinical allergy*. *Clin Exp Immunol* 2008;153: 10-18.
19. Zuberbier T, Asero R, Bindslev Jensen C, Walter Canonica G, Church MK, Giménez-Arnau AM. Management of urticaria. *Allergy* 2009;64:1427-43
20. Zuberbier T. Urticaria. *Allergy* 2003;58: 1224-34.

Address for Corresponding Author:
Dr. Ashfaq Ahmad Shah Bukhari ,
Assistant Professor of Physiology,
Rehman Medical College, Peshawar
Contact #: 03229046788