The Treatment of chronic recurrent urticaria with Fexofenadine and Hydroxyzine Hcl in Libyan patients.

Abstract

Introduction: Chronic recurrent urticaria characterized by short-lived circumscribed erythematous, edematous and itchy wheals usually lasting for a few hours to few days for a period of at least six weeks or more, without an identifiable causes and its negative influence on the quality of life. It's a disabling affliction that considerably limits patients' daily activities.

Fexofenadine hydrochloride is a carboxylated metabolic derivative of terfenadine and third generation selective histamine H1-receptor antagonist with non-sedative effects. Hydroxyzine Hcl (Atarax) is a antihistamine H1 blocker with anticholinergic and sedative propertiesand relieving the symptoms of allergy..

Objective: To access efficacy and safety of a combined administration of the Fexofenadine and Hydroxyzine Hcl in the treatment of chronic recurrent urticaria.

Patients and Methods:

In this study was conducted in 48 Libyan patients, the mean age was 37 years (21-65 years). 22 females and 26 males, all patients with a diagnosis of chronic recurrenturticaria, the average duration of the disease was 6months (4-10months) during the time period from January 2016 to December 2016. All our patients were investigated and examined to rule out any causes.

The patients were received fexofenadine 120mg per daytime and hydroxazine 25mg at bedtime for 3 weeks.

Result: The a combination of fexofinadine and Hydroxyzine provides to be effective against urticarial symptoms in our forty-eight patients with recurrent chronic urticaria (good response in 16patients (33%) and very good response in18 patients (37,5%) satisfactory in 8 patients(17%) and in 6 patients(12,5%)unsatisfactory). Good tolerance of a combination fexofinadine and Hydroxyzine in our patients was reported.

Conclusion: The a combination of fexofenadine and hydroxazine appears to be an effective and safety treatment of chronic recurrent urticaria that improves urticarial symptoms and quality of life. And might benefit patients who do not respond to single anti-allergic drug.

Keywords: Fexofenadine, Hydroxyzine, Chronic recurrent urticaria, Quality of life.

Introduction: Chronic recurrent urticaria characterized by short-lived circumscribed erythematous, edematous and itchy wheals usually lasting for a few hours to few days for a period of at least six weeks or more, without an identifiable causes and its negative influence on the quality of life. It's a disabling affliction that considerably limits patients' daily activities.

Chronic idiopathic urticaria (CIU) is defined by the almost daily presence of urticaria for at least six weeks without an identifiable cause. Symptoms include short-lived wheals, itching and erythema. There is limited data available comparing the effects of fexofenadine with other antihistamines in chronic idiopathic urticaria from India. The aim of this study was to investigate the efficacy and side-effects of the combination fexofenadine and hydroxazine in patients with chronic idiopathic urticaria..(6-12).

Fexofenadine hydrochloride, the major active metabolite of terfenadine, is an antihistamine with selective H1-receptor antagonist activity. Both enantiomers of Fexofenadine hydrochloride displayed approximately equipotent antihistaminic effects. Fexofenadine hydrochloride inhibited antigen-induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats(9-11). The clinical significance of these findings is unknown. In laboratory animals, no anticholinergic or alpha1-adrenergic blocking effects were observed. Moreover, no sedative or other central nervous system effects were observed. Fexofenadine does not cross the blood-brain barrier.

fexofenadine hydrochloride is a carboxylated metabolic derivative of terfenadine and third generation selective histamine H1-receptor antagonist with antihistaminic and non-sedative effects. Fexofenadine competitively binds peripheral H1-receptors, thereby stabilizing an inactive conformation of the receptors.

Fexofenadine hydrochloride is a nonsedating long-acting antihistamine with highly selective peripheral H1 receptor antogonist activity and a 120 mg once daily dose showed optimum effects in chronic urticaria. (1) (12).

Hydroxyzine Hcl (Atarax) is a antihistamine with anticholinergic and sedative properties and relieving the symptoms of allergy that works by blocking histamine receptors, thereby stopping the actions of histamine.

In this study was conducted in 48 Libyan patients, the mean age was 37 years (21-65 years). 22 females and 26 males, all patients with a diagnosis of chronic recurrent urticaria, the average duration of the disease was 6 months (4-10months) during the time period from January 2016 to December 2016. All our patients were investigated and examined to rule out any causes.

The patients were received fexofenadine 120 mg per daytime and Hydroxyzine 25mg at bedtime for 3 weeks.

Hydroxyzine Hcl (Atarax) is a antihistamine with anticholinergic and sedative properties and relieving the symptoms of allergy that works by blocking histamine receptors, thereby stopping the actions of histamine.

Objective: To access efficacy and safety of a combination the Fexofenadine and Hydroxyzine Hcl in the treatment of chronic recurrent urticaria.

Patients and Methods: In this prospective study was conducted in 48 Libyan patients the mean age was 37 years (21-65 years),(Fig:2). 22 females and 26 males (Fig:1).all patients with a diagnosis of chronic recurrent urticaria, the average duration of the disease was 6months (4-10months) during the time period from January 2016 to December 2016.(Fig:3).

All our patients were investigated and examined to rule out any causes.

The patients were received fexofenadine 120mg per daytime and atarax 25mg at bedtime for 3 weeks.

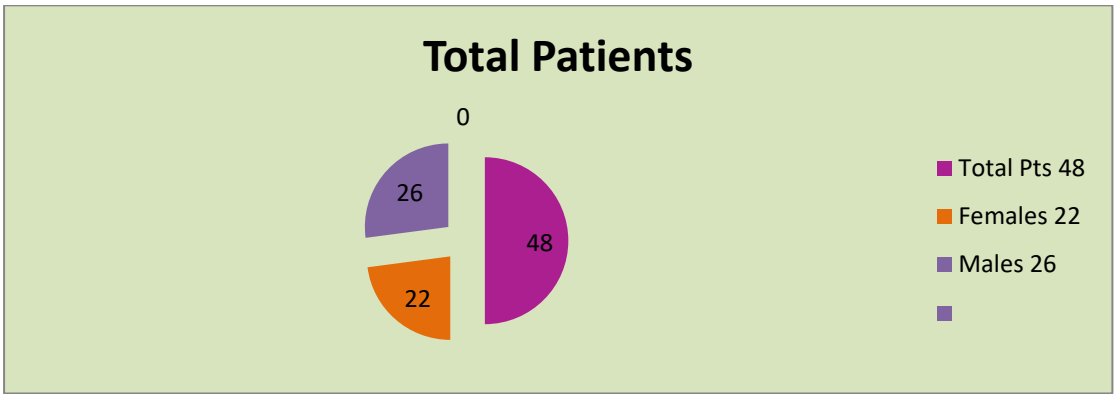

Figure: (1).

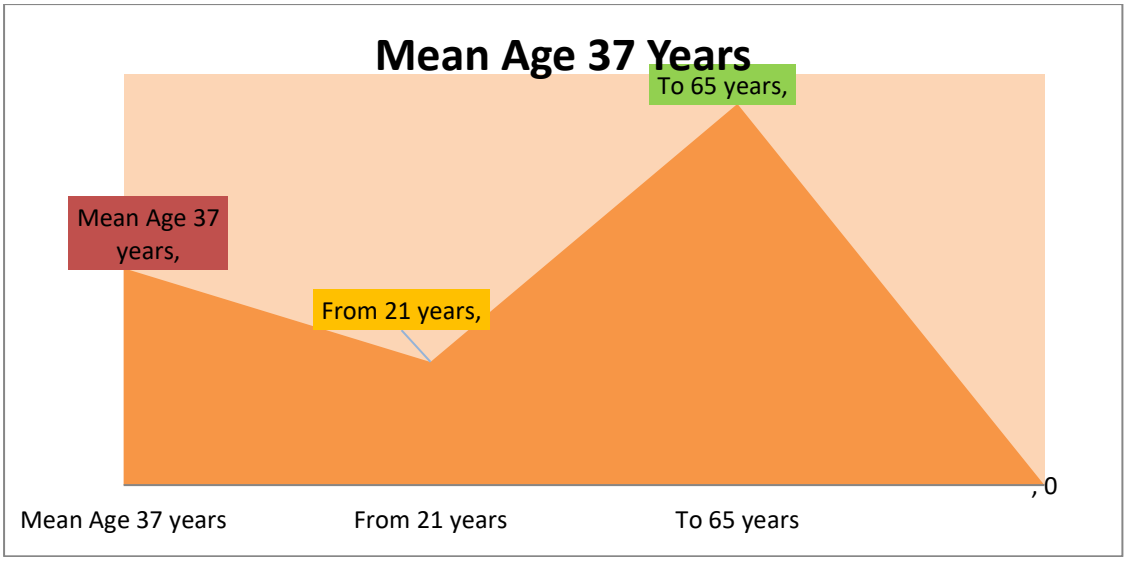

Figure: (2).

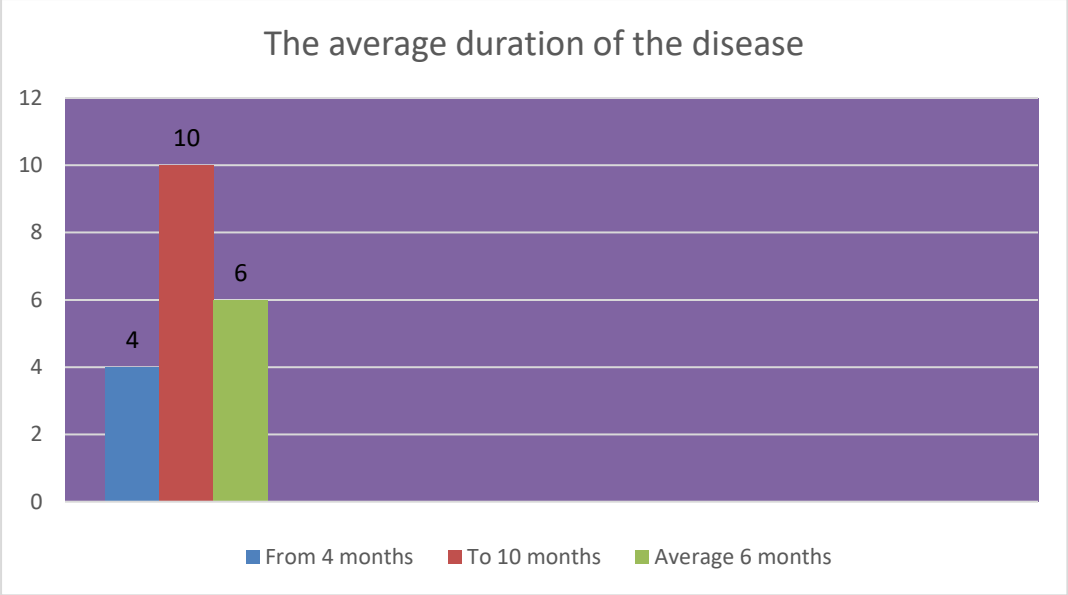

Figure: (3).

Result:
Combined administration of fexofinadine and Hydroxyzine Hcl provides to be effective against urticarial symptoms in our forty-eight patients with recurrent chronic urticaria (good response in 16 patients (33%) and very good response in18 patients (37,5%) satisfactory in 8 patients(17%) and in 6 patients(12,5%)unsatisfactory) (Fig:4). Good tolerance of a combination fexofinadine and Hydroxyzine in our patients was reported. Adverse event that is usually mild and transient and did not require the drugs withdrawal (sleepiness in 14 patients.(29%) (Fig:5)..Combined administration of fexofinadine and Hydroxyzine can be recommended for chronic recurrent urticaria and wide application in therapy of allergic diseases.

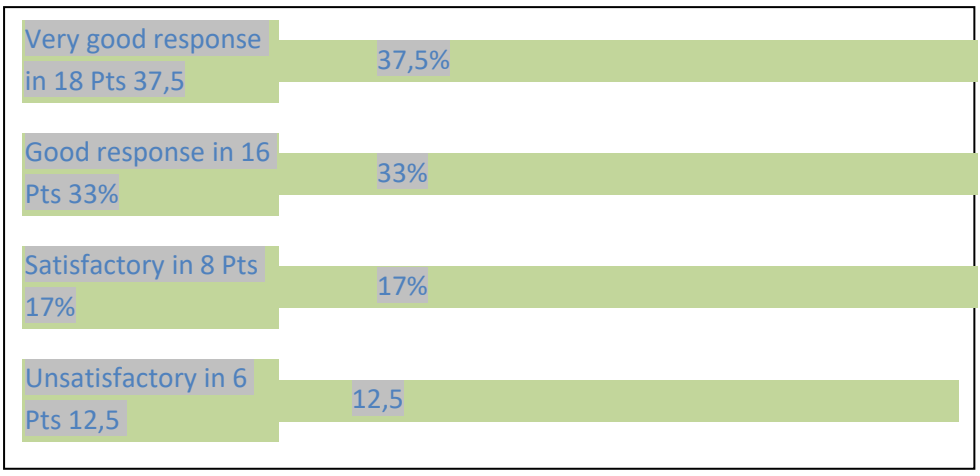

Figure: (4A).

Figure: (4B).

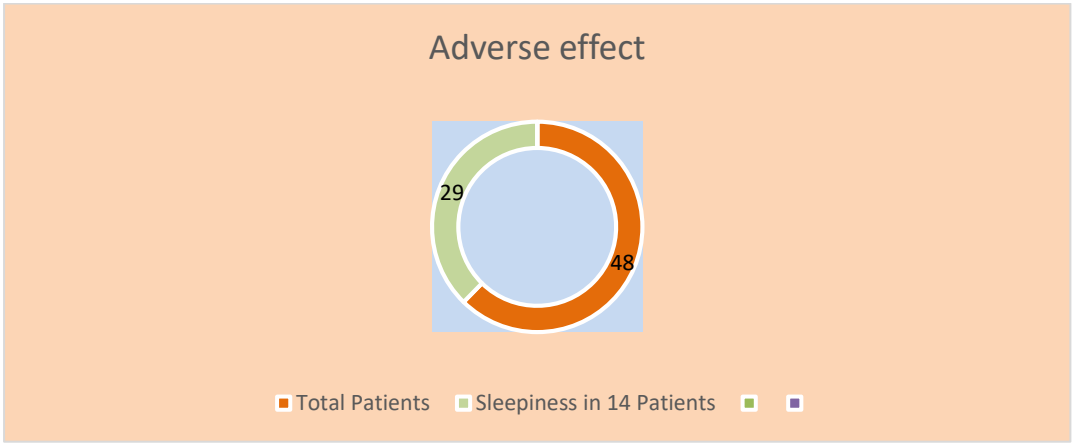

Figure: (5).

Discussion:

Chronic idiopathic urticaria (CIU) is defined by the almost daily presence of urticaria for at least six weeks without an identifiable cause. Symptoms include short-lived wheals, itching and erythema. There is limited data available comparing the effects of fexofenadine with other antihistamines in chronic idiopathic urticaria from India. The aim of this study was to investigate the efficacy and side-effects of the combination fexofenadine and hydroxazine in patients with chronic idiopathic urticaria, (12). Additionally, Urticaria is a cutaneous syndrome characterized by dermal edema (wheal) and erythema (flare) that blanches with pressure. The lesions typically last less than 24 hours and are usually pruritic. In 1983, Christensen and Maibach summarized the theory behind the use of histamine H1 receptor antagonists

(antihistamines) in clinical dermatology. These agents remain the mainstay of treatment for urticaria.

Fexofenadine hydrochloride, the major active metabolite of terfenadine, is an antihistamine with selective H1-receptor antagonist activity. Both enantiomers of Fexofenadine hydrochloride displayed approximately equipotent antihistaminic effects. Moreover, Fexofenadine hydrochloride inhibited antigen-induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats. The clinical significance of these findings is unknown. In laboratory animals, no anticholinergic or alpha1-adrenergic blocking effects were observed. However, no sedation or other central nervous system effects were observed. Fexofenadine does not cross the blood-brain barrier.(11).

Fexofenadine hydrochloride is a nonsedating long-acting antihistamine with highly selective peripheral H1 receptor antogonist activity and a 120 mg once daily dose showed optimum effects in chronic urticaria**.**(1).

In addition, Hydroxyzine Hcl (Atarax) is a antihistaminewith anticholinergic and sedative propertiesand relieving the symptoms of allergy that works by blocking histamine receptors, thereby stopping the actions of histamine.(14).

Older antihistamines, such as hydroxyzine and chlorpheniramine, are effective in the treatment of urticarias, but they also have marked sedative and anticholinergic effects.

These articles reviews the medical literature on the effectiveness of antihistamines in urticarial syndromes, including acute, chronic idiopathic and the physical urticarias.

In our study was conducted in 48 Libyan patients, the mean age was 37 years (21-65 years), Twenty two females and Twenty six males(Fig:1,2). All patients with a diagnosis of chronic recurrent urticaria, the average duration of the disease was 6months (4-10months) during the time period from January 2016 to December 2016.(Fig:3). All our patients were investigated and examined to rule out any causes. The patients were received fexofenadine 120mg per daytime and hydroxazine 25mg at bedtime for 3 weeks.

In accordance to our present work were included Forty eight patients in the age group of 21 to 65 years with CIU were administrated fexofenadine 120 mg once daily in the morning and hydroxazine 25mg once daily in at bedtime. Physical urticaria patients, pregnant women and lactating mothers were not included. All the patients were investigated thoroughly to rule out any septic focus or any obvious cause of urticaria and their complete blood count, urine and sugar were analyzed before starting the treatment. A general and systemic examination was conducted and their consent was obtained at the initial visit. Treatment was given either up to the relief of symptoms or up to three weeks. All patients were followed up for response to treatment. All patients were reviewed at 0, two and three weeks with urticaria activity score.

Moreover, the Urticaria Activity Score consisted of the sum of the wheal number score and the itch severity score (1,3). The wheal numbers are graded from 0 to 3 as follows: 0 - less than 10 small wheals (diameter, <3 cm); 1-10 to 50 small wheals or less than 10 large wheals (diameter, >3 cm); 2 - greater than 50 small wheals or 10 to 50 large wheals; and 3 - almost the whole body is covered.

Whereas the severity of the itching is graded from 0 to 3 (0, none; 1, mild; 2, moderate; and 3, severe).

At the end of thethird week of this combination therapy has shown the decrease in urticarial activity scores: was 87.5%(a good responded in 16 patients (33%) and very good response in18 patients (37,5%) satisfactory in 8 patients(17%) in this

combination therapy. Therefore, Fexofenadine and atarax treatment was decreased urticarial activity scores significantly, No patient could stop treatment before three weeks of treatment.

Even so, in other single anti-allergic study, was a randomized, double-blind, placebo-controlled, parallel, multicenter research has shown the hydroxazine25 mg once daily at bedtime, is an effective treatment for CIU, characterized not only by a rapid and sustained response, but also by an important improvement in Quality of life. (2). However similarly fexofenadine 120 mg once daily is well tolerated and is statistically superior to placebo in reducing signs and symptoms of CIU and in ameliorating interference with sleep and daily activities due to urticaria. However, our results are in accordance with some previous single anti-allergic therapy studies.(13-19). Whereas Day JH, Briscoe MR Welsh A, et al.were demonstrated that fexofenadine HC1 at a single daily oral dose of 120mg is an effective non-sedating antihistamine for the treatment of CIU and is devoid of any significant adverse effect including cardiotoxicity.

So far there is not much published data available on 120mg fexofenadine molecule. Most of the studies address the efficacy and safety parameters of fexofenadine in seasonal allergic rhinitis and asthma.(8).

Despite of in our study majority of the patients were between 25 to 55 years of age and males outnumbered females, it is in corroboration with the earlier observations that CIU mostly affects adults and males (3.5). There was improvement in TSS in all the patients. The baseline TSS (total symptom score) (TSS)(came down to '0' by the end of 3 weeks. However, there was no correlation between the baseline TSS and degree of improvement.

The most distressing symptom of CIU is pruritus. It is generally recognized that a combination of sedating and non-sedating H1 receptor antagonists are more effective in controlling the pruritus than the wheals, there agrees with our study. (7,8,9).Whereas a review of the literature reveals that there are few studies which document the efficacy of first and second-generation antihistamines in the treatment of urticaria, a biologic entity that usually resolves within 3-4 weeks. We did not identify controlled studies that suggested superiority of any antihistamine in the treatment of urticaria.(20),(21),(22).

However in our present study the drug controlled the pruritus and wheals, effectively at the end of thethird week the decrease in urticaria activity scores was 87.5%,(good response in 16 patients (33%) and very good response in18 patients (37,5%) satisfactory in 8 patients(17%).Combined administration of Fexofenadine and atarax in the treatment of chronic recurrent urticaria was significantly decreased activity scores of urticarial lesions and symptoms and no patient could stop treatment before third week of treatment.This was in corroboration with the study by Paul et al.(1) Fexofenadine was well tolerated throughout the study period (6). Adverse effects were analyzed that is usually mild and transient and did not require the drugs withdrawal (sleepiness in 14 patients)(29%).(9-10).

In fact, Our study found the combination of fexofenadine and hydroxazine superior to mono-therapy at the end of the third week in treatment of chronic idiopathic urticaria. Nevertheless, There are no studies comparing the combination fexofenadine and hydroxazine in treatment of CIU. Large studies are required to confirm these findings.

Conclusion: The a combination of fexofenadine and hydroxazine (Atarax) appears to be an effective and safety treatment of chronic recurrent urticaria that improves

urticarial symptoms and quality of life. And might benefit patients who do not respond to single anti-allergic drug.
However, Antihistamines are the mainstay of urticarial therapy. This evidence-based review suggests that there are efficacy differences between newer, non-sedating antihistamines and older agents in some forms of the disorder. Clearly, further well-controlled clinical trials in larger numbers of patients are needed to clarify the role of these agents in the treatment of urticaria.

References:

1. Paul E, Berth Jones J, Ortonne JP. Fexofenadine hydrochloride in the treatment of chronic idiopathic urticaria: A placebo controlled parallel group, close ranging study. J Dermatol Treatment 1998;9:143-9.
2. Kapp A, Pichler WJ. Fexofenadine is an effective treatment in patients suffering from chronic idiopathic urticaria: A randomized, double-blind, placebo-controlled, parallel, multicenter study. Int J Dermatol 2006;45:469-74
3. Finn AF Jr, Kaplan AP, Fretwell R, Qu R, Long J. A double-blind, placebo-controlled trialof fexofenadine HCl in the treatment of chronic idiopathic urticaria. J Allergy ClinImmunol 1999;104:1071-8.
4. O' Donnell BF, Lawlor F, Simpson J, et al. The impact of chronic .4
.urticaria on the quality of life. Br J Dermatol 1997;136:197-201
5. Bllehen SS, Thomas SE, Greaves MW, et al. sedating and non-sedating .5
antihistamines in the treatment of chronic idiopathic urticaria: a multicentre
.randomized double blind study. Br J Dermatol 1987;319:81-48
6. Soter NA. Urticaria: current therapy. J Allergy ClinImmunol 1990;86:1009- .6
1014.
.7. Markham A, Wagstaff AJ. Fexofenadine. Drugs 1998;55:269-2747. .
8. Day JH, Briscoe MR Welsh A, et al. Onset of action, efficacy and .8
safety of a single dose of fexofenadine hydrochloride for ragweed allergy using an environmental exposure unit. Ann Allergy Asthma Immunol 1997;79:533-
.540
9. Rampe D, Wible B, Brown AM, et al. Effects of terfenadine and its .9
metabolites on delayed rectifier K+ channel cloned from human heart.
.MolPharmacol 1995;123:1240-1245
10. Dhar S, Hazra PK, Malakar S, et al. Fexofenadine induced QT .10
.prolongation - a myth or fact? Br J Dermatol 2000;142:1-3
11. Woosley RL, Chen Y, Freiman JP, et al. Mechanism of the .11
.fexofenadine actions, JAMA 1993;269:1532-1536
12. Greares MW. Antihistamines treatment, a patient self assessment .12
.method in chronic urticaria. Br Med J 1981;283:1435-1436
13. Nelson HS, Reynolds R, Mason J. Fexofenadine HCl is safe and effective .13
for treatment of chronic idiopathic urticaria. Ann Allergy Asthma Immunol 2000; 84:517–522
14. Boggs P.B., Ellis C.N., Grossman J., et al. Double-blind, placebo- .14
controlled study of hydroxyzine in patients with chronic idiopathic urticaria. Ann Allergy 1989; 63: 616–620
15. Kalivas J., Breneman D., Tharp M., et al. Urticaria: clinical efficacy of .15
cetirizine in comparison with hydroxyzine and placebo. J Allergy ClinImmunol 1990; 86: 1014–1018

16. Monroe E.W. Relative efficacy and safety of hydroxyzine, and placebo in .16
chronic idiopathic urticaria. ClinTher 1992; 14 (1): 17–21
17. Salo O.P., Harvey S.G., Calthrop J.G., et al. A comparison of acrivastine .17
versus hydroxyzine and placebo in the treatment of chronic idiopathic urticaria. J
.Int Med Res 1989; 17 Suppl. 2: 18B–2 lB
18. Kobza Black A., Aboobaker J., Gibson J.R., et al. Acrivastine versus .18
hydroxyzine in the treatment of cholinergic urticaria. A placebo-controlled study.
ActaDermVenereol 1988; 68 (6): 541–544
19. Neittaanmaki H., Myohanen T., Fraki J.E. Comparison of cinnarizine, .19
cyproheptadine, doxepin, and hydroxyzine in treatment of idiopathic cold
.urticaria: usefulness of doxepin. J Am AcadDermatol 1984; 11 (3): 483–489
20. Christensen O.B., Maibach H.I. Antihistamines in dermatology. .20
SeminDermatol 1983; 2: 270–280
21. Matthews K.P. Chronic urticaria. In: Schocket A.L. editor. Clinical .21
management of urticaria and anaphylaxis,New York: Marcel Dekker 1993;21,68
22. Simons F.E.R. Antihistamines. In: Middleton E., Ellis E.F., Yunginger .22
J.W., et al., editors. Allergy: principle and practice. 5th ed. St Louis (MO):
Mosby-Year Book, Inc., 1998: 613