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Original Research Article

Aetiopahogenesis and management of chronic urticaria -A Study

Rashmi Rani[1], Dharmendra Kumar[1,*]

[1] *Dept. of Dermatology, Narayan Medical College and Hospital, Jamuhar, Bihar, India*

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ABSTRACT

Introduction: Urticaria more commonly known as " Nettle rash " or hives, presents as circumscribed, raised (oedematous), usually pruritic evanescent skin lesions. The lesions may be pink or red, although classifiably they are pale wheals surrounded by an erythematous flare. Approximately 15% to 20% of the general population will have urticaria at least once during their lifetime. Persons of any age may experience urticaria and/or angioedema.

Materials and Method: 150 cases of chronic urticaria of both sexes and of different age group were selected from the out patient department of Dermatology, Narayan medical college Sasaram Bihar. Cases having more than 6 weeks of duration of disease were included in the study.

Result: The maximum no of cases were seen in the age group of 25-34 years (34.6%), in 35-44 years no cases are 25.4%, 21.4% in age group 15-24 yrs and 18.6% in age group 45-55. duration of chronic urticaria ranging from 6 weeks to 24 months. Maximum numbers of cases (66.67%) were having duration up to 12 months. Only 33.33% were having duration more than 12 months

Discussion and Conclusion: Maximum number of patients presented with the duration of disease of 12 months.

Finding suggest association of cyst of Amoeba and Giardia in some cases. Raised serum TSH and IgE level was seen in some cases. Non veg diet especially fish was associated with Chronic Urticaria.

Antihistamines are the most effective and preferred drug for the treatment of Chronic Urticaria.Traditional antihistaminic (hydroxyzine) and second generation antihistamines (levocetrizine and fexofenadine) was prescribed in therapeutic dosages and there results were interpreted.

1. Introduction

Urticaria (from the Latin word urtica, (to burn) or hives), are a kind of skin rash notable for dark red, raised, itchy bumps. The lesions may be pink or red, although classifiably they are pale wheals surrounded by an erythematous flare. The superficial swelling s of dermis are called wheals, A wheal consists of three typical features: (i) a central swelling of variable size; (*ii*) an associated itching or sometimes burning; and (*iii*) a fleeting duration of usually 1–24 hr. Urticaria may be associated with angioedema. Angioedema is the deeper swelling of the dermis or subcutaneous and /or sub mucosal tissue. It is sometimes painful and resolution is slower than wheals (up to 72 h). The individual lesions of urticaria arise suddenly and rarely persist more than 24hr.

Urticarial wheals are variable in size ranging from a few millimetres to 6-8 inches in diameter (giant urticaria). Lesions may appear anywhere on the body including scalp, palm and soles. In 50% of cases urticaria is associated with angioedema (yadav s.et al 2006). 10% of patients experience only angioedema without hives and 40% exhibit wheals alone (Bagenstose SE, Fortson JS, Luquin E et al) [1,2]

The itching of urticaria is almost invariable, although some patients have more intense pruritis than others. Patients tend to rub rather than scratch, hence excoriation marks are not seen. Itching is usually worse in the evening or night. There may be pricking and burning sensation. [3]

* *Corresponding author*.
E-mail address: dharma_derma@yahoo.co.in (D. Kumar).

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Approximately 15% to 20% of the general population will have urticaria at least once during their lifetime. Person s of any age may experience urticaria and/or angioedema. The urticaria occurs most frequently after adolescence with the highest incidence in young adults. The exact incidence and prevalence of urticaria are not known, although it occurs in at least 0.1% and possibly up to 3% of the populations. Acute urticaria is more common in children. (Greaves MW et al)[4]

2. Aims and Objectives

To study the aetiopathogenesis and management of chronic Urticaria.

3. Materials and Methods

The present study " etiopathogenesis and management of chronic urticarial - a study" was carried out on the patients attending the out patient department of skin, VD and leprosy Narayan medical college Sasaram Bihar from January 2017 to September 2019.

3.1. Case selection

150 cases of chronic urticaria of both sexes and of different age group were selected from the out patient department of Dermatology, Narayan medical college Sasaram Bihar. Cases having more than 6 weeks of duration of disease were included in the study.

The following criteria excluded patients from enrolment in study:

Pregnant and lactating mother, patients who were on corticosteroid, patients of cardiovascular or hepatorenal disease were also excluded. The object of the study was fully explained to each patient in the initial visit and consent was taken from every patient. All the cases were thoroughly examined in natural day light.

The following line of treatment was adopted.

[A] General Management: Every patient was reassured. The nature and purpose of study were fully explained to the patients. They were asked to withhold their previous medications including steroid, leucotrine receptor antagonist, methotrexate,anti-histamines etc 48 hours before starting the trial considering there effect will taper.

[B] Drugs: With a view to evaluate the efficiency and side effects of drugs, 150 patients were randomly divided into 3 groups, each group consisting of 50 patients.

Table 1: Group A: (n=50)

No of patients	Drug used
25	Hydroxyzine alone
25	Hydroxyzine + Ranitidine

The 25 patients were treated with Hydroxyzine 25 mg alone and 25 patients were treated with Hydroxyzine 25 mg at bed time plus Ranitidine 150 mg twice daily.

Table 2: Group B:(n=50)

No of patients	Drug used
25	Levocetrizine
25	Levocetrizine + Ranitidine

The 25 patients were treated with Levocetrizine 5 mg alone and rest 25 patients were on Levocetrizine 5mg plus Ranitidine 150 mg twice daily.

Table 3: Group C :(n=50)

No of patients	Drug used
25	Fexofenadine alone
25	Fexofenadine + Ranitidine

The 25 patients were treated with Fexofenadine 150 mg single dose and rest of 25 were on Fexofenadine 150 mg single doze plus Ranitidine 150 mg twice daily.

Criteria for evaluation of response-

The patients in each group were assessed every week during treatment (1 month) and were followed up to 1 month after stopping the drug

The patients were assessed in two ways, one by the doctor at each visit and another by the patient himself or herself.

All patients were analysed for the side effects of the drugs like.sedation, dry mouth, G.I.T disturbance and increase appetite etc.

Assessment is done with the help of Urticaria Activity Score.

Subjective evaluation (pruritus)

Table 4:

Score	Pruritus	Response
0	None	Excellent
1	Mild, not troublesome	Good
2	Troublesome but not interfere with sleep	Fair
3	Severe pruritus,Interfere with normal daily activity and sleep	Poor

Table 5: Objective Evaluation (Wheals)

Score	Wheals	Response
0	None	Excellent
1	Mild(<20 wheals/24 hr)	Good
2	Moderate(20-50 Wheals/24 hr)	Fair
3	Intense(>50 Wheals/24 hr)	Poor

3.2. Observation

The maximum no of cases were seen in the age group of 25-34 years (34.6%), in 35-44 years no cases are 25.4%, 21.4

Table 6: Age Distribution

Age in yrs	No of patients	Percentage
15 – 24	32	21.4
25 – 34	52	34.6
35 – 44	38	25.4
45 – 55	28	18.6
Total	150	100

% in age group 15-24 yrs and 18.6% in age group 45-55.

Table 7: Sex distribution

Sex	No of patients	Percentage
Male	54	36
Female	96	64
Total	150	100

The above table shows that out of 150 patients 54 were male (36%) and 96 were female (64 %). Chronic urticaria was found more common in females than males.

Table 8: Duration of disease

Duration of disease	No. of patient	Percentage
6 weeks to 6 months	54	36
7 months to 12 months	46	30.67
13 months to 18 months	32	21.33
19 months to 24 months	18	12
Total	150	

The above table shows the duration of chronic urticaria ranging from 6 weeks to 24 months. Maximum numbers of cases (66.67%) were having duration up to 12 months. Only 33.33 % were having duration more than 12 months.

Table 9: Food habits

Diet	No of patients	Percentage
Vegetarian	72	48
Non vegetarian	78	52
Total	150	100

No significant variation was observed in dietary habits of chronic urticaria. But it shows that its incidence was slightly high in patients taking non vegetarian diet.

Table 10: Number of lesions

Number of lesions	Number of patients	Percentage
1 to 20	60	40
20 to 40	52	34.7
More than 40	38	25.3

The above table shows that in 60 patients (40%) the number of lesions varied from 1 to 20,in 52 patients 20 to 40 lesion(34.7%), and in 38 patients more than 40 lesion (25.3). In majority of cases 74.7%, the number of lesion were less than 40. Number of wheels are counted although sizes were varied to some extent.

Table 11: Laboratory Finding (n=150)

Investigations	Normal	Elevated
Total W.B.C count	97%	3%
Differential count		
neutrophils	100%	0%
lymphocytes	96%	4%
monocytes	100%	0%
eosinophils	93%	7%
basophils	100%	0%
ESR	96%	4%
Serum TSH	89%	11%
Routine urine examination	100%	0%
Hepatitis B Ag	100%	0%

Stool examination was done in 50 patients. Out of which in 4 patients (8%) cysts of Amoeba and Giardia were found which was excluded from study. As it is self financed project the auto immune cause of chronic urticaria was excluded clinically. Serum TSH was done to evaluate subclinical thyroid disorder.

The above table shows that out of 25 patients (Hydroxyzine alone) 5 patients (20%) achieved excellent response, 4 patients (16 %) showed good response, 6 patients (24%) showed fair response and 10 patients (40%) showed poor response.

In rest 25 patients (Hydroxyzine+ Ranitidine) 6 patients (24%) achieved excellent response, 5 patients (20%) showed good response, 7 patients (28%) showed fair response and 7 patients (28%) showed poor response. These responces were evaluated by dermatologist in subsequent visit of the patient which was planned.

The above table shows that out of 25 patients with Levocetrizine 5mg alone 8 patients (32%) achieved excellent response, 6 patients (24%) showed good response, 7 patients (28%) showed fair response and 4 patients (16%) showed poor response.

In rest 25 patients (Levocetrizine 5mg + Ranitidine 150mg/d) 9 patients (36 %) achieved excellent response,7 patients (28%) showed good response, 8 patients (32 %) showed fair response and 1 patients (4%) showed poor response.

The above table shows that out of 25 patients with Fexofenadine 180 mg/d alone 7 patients (28%) achieved excellent response, 5 patients (20%) sh owed good response, 5 patients (20%) showed fair response and 8 patients (32%) showed poor response.

In rest 25 patients (Fexofenadine 180 mg/d + Ranitidine 150mg twice/d) 8 patients (32%) achieved excellent response, 6 patients (32%) showed good response, 7 patients (28%) showed fair response and 4 patients (16%) showed

Table 12: Therapeutic response Group A

Grade of response	Pts.showing response in Hydroxyzine alone	percentage	pts.Showing response in Hydroxyzine+ Ranitidine	percentage
Excellent=0	5	20%	6	24%
Good=1	4	16%	5	20%
Fair=2	6	24%	7	28%
Poor=3	10	40%	7	28%
	25	100%	25	100%

Table 13: Therapeutic response Group B

Grade of response	pts.showing response in levocetrizine alone	percentage	pts.showing response in levocetrizine+ Ranitidine	Percentage
Excellent=0	8	32%	9	36%
Good=1	6	24%	7	28%
Fair=2	7	28%	8	32%
Poor=3	4	16%	1	4%
	25	100%	25	100%

Table 14: Therapeutic response Group C

Grade of response	Pts.showing response in fexofenadine	Percentage	Pts.showing response in fexofenadine+ Ranitidine	Percentage
Excellent=0	7	28%	8	32%
Good=1	5	20%	6	24%
Fair=2	5	20%	7	28%
Poor=3	8	32%	4	16%
	25	100%	25	100%

Table 15: Relative response Group A to Group C With only H1 antihistamine

Response	Gr-A(Hydroxyzine)	Gr-B(Levocetrizine)	Gr-C(Fexofenadine)
Excellent=0	5(20%)	8(32%)	7(28%)
Good=1	4(16%)	6(24%)	5(20%)
Fair=2	6(24%)	7(28%)	5(20%)
Poor=3	10(40%)	4(16%)	8(32%)

poor response.

The above table shows that excellent response were 32% with Levocetrizine while 28% in case of Fexofenadine and 20% in case of Hydroxyzine.

Good response were present in 24% with Levocetrizine while 20 % in case of Fexofenadine and 16% in case of Hydroxyzine.

Fair response were present in 28 % with Levocetrizine while 20% in case of Fexofenadine and 24% in case of Hydroxyzine.

16% of cases showed poor response in case of Levocetrizine while 32% in case of Fexofenadine and 40% in case of Hydroxyzine.

The above table shows that excellent response were 36% with Levocetrizine+ Ranitidine while 32% in case of Fexofenadine+ Ranitidine and 24% in case of Hydroxyzine+ Ranitidine.

Good response were present in 28% with Levocetrizine+ Ranitidine while 24% in case of Fexofenadine+ Ranitidine and 20% in case of Hydroxyzine+ Ranitidine.

fair response were present in 32% with Levocetrizine+ Ranitidine while 28% in case of Fexofenadine+ Ranitidine and 28% in case of Hydroxyzine+ Ranitidine.

4% of cases showed poor response in case of Levocetrizine+ Ranitidine while16% in case of Fexofenadine+ Ranitidine and 28% in case of Hydroxyzine+ Ranitidine.

Table shows that sedation was the commonest side effect in Hydroxy zine treated patients 37 out of 50 patients (74%) reported sedation.

Sedation was least in Fexofenadine group only 4%. In levocetrizine treated patients it was 24%.

Dry mouth was reported in 13 patients (26%) in Hydroxyzi ne treated patients. While it was 3(6%) in levocetrizine treated patients.

Headache was reported in 3(6%) in Hydroxyzine treated patients. While it was 1(2%) Fexofenadine group.

Constipation was complained in 8(16%) in Hydroxy zine treated patients. While it was 2(4%) in levocetrizine treated

Table 16: Relative response Group A to Group C With H1+H2 antihistamine

Response	Gr-A (Hydroxyzine+Ranitidine)	Gr-B (Levocetrizine+ Ranitidine)	Gr-C (Fexofenadine+ Ranitidine
Excellent=0	6(24%)	9(36%)	8(32%)
Good=1	5(20%)	7(28%)	6(24%)
Fair=2	7(28%)	8(32%)	7(28%)
Poor=3	7(28%)	1(4%)	4(16%)

Table 17: Side effects Group A to Group C

Side effects	Group A	Group B	Group C
Sedation	37(74%)	12(24%)	2(4%)
Dry mouth	13(26%)	3(6%)	0
Headache	3(6%)	0	1(2%)
Constipation	8(16%)	2(4%)	0

patients.

4. Discussion

The present study was undertaken for better management strategy in case of chronic urticaria. Different drug combinations were used for better result. First generation H1 antihistamines alone and in combination with H2 receptor blocking drug were used. Different second generation H1 receptor antihistamines alone and in combination with H2 receptor blocking drug were used. A comparative therapeutic efficacy of different drugs and their combinations is presented.

In present study we have observed that there is female predominance and commone in second and third decade of life. In most of cases duration was more than one year. This finding corroborates with the study of Joseph N et al.[5]

4.1. Treatment

In the present study Table no 6 shows Hydroxy zine 25 mg/day for 4 weeks in 25 patients of chronic urticaria. As per the table 20% show excellent result, 16% show good, 24% show fair result and rest 40% shows poor response. In Hydroxyzine combined with Ranitidine, 24% show ed excellent result, 20% showed good, 28% showed fair result and rest 28% showed poor response.

The result of Levocetrizine alone, 32% show ed excellent response, 24% showed good, 28% showed fair response and rest 16% showed poor response. Levocetrizine combined with Ranitidine, 36% show ed excellent response, 28% showed good, 32% showed fair response and rest 4% showed poor response.

(Table 14) Fexofenadine (180mg/day) alone, 28% show ed excellent response, 20% showed good, 20% showed fair response and rest 32% showed poor response. Fexofenadine combined with Ranitidine, 32% showed excellent response, 24% showed good, 28% showed fair response and rest 16 % showed poor response.

The above data shows that H1 antihistaminic combined with H2 antihistamines shows the greater efficacy than the H1 antihistaminic alone. Human skin blood vessels possess H2 receptors, as well as the commonly recognized H1 receptors,suggesting a possible reason for the frequent failure of H1 antihistamines in controlling this disorder.[6]

My study indicates that combined H1 and H2 antihistamine therapy is statistically more effective than H1 antihistamines alone in controlling the symptoms of chronic urticaria

Urticaria activity scores were improved significantly among those receiving therapy with the H1- antihistamine plus the H2-antihistamine. (Wan KS et al).[7]

Other experts consider the combination to be safe and affordable, sometimes effective, and preferable in its risk-benefit profile to other second-line treatment options (Sussman GL, Simons KJ et al).[8]

4.2. Comparative Response

Table 14 shows excellent response, 32% in case of Levocetrizine, 28% in Fexofenadine and 20% in case of Hydroxyzine.

Table 16 shows excellent response, 36% in case of Levocetrizine+Ranitidine, 32% in Fexofenadine+Ranitidine and 24% in case of Hydroxyzine+Ranitidine.

Good response, 24% in case of Levocetrizine, 20% in Fexofenadine and 16% in case of Hydroxy zine (Table 15). Good response, 28% in case of Levocetrizine+Ranitidine, 24% in Fexofenadine+Ranitidine and 20% in case of Hydroxyzine+Ranitidine (Table 17).

Fair results, 28 % in case of Levocetrizine, 24% in Fexofenadine and 20% in case of Hydroxyzine (Table 14). Good response, 32% in case of Levocetrizine+Ranitidine, 28% in Fexofenadine+Ranitidine and 28% in case of Hydroxyzine+Ranitidine (Table 17).

Poor response, 16 % in case of Levocetrizine, 32% in Fexofen adine and 40% in case of Hydroxyzine (Table 9). Poor response, 4% in case of Lev ocetrizine+Ranitidine,

16% in Fexofenadine+Ranitidine and 28% in case of Hydroxyzine+Ranitidine (Table 17).

The present study showed excellent to fair response in 84% patients with Levocetrizine alone and 96% when combined with H2 antihistamines.

Fexofenadine alone showed excellent to fair response in 68% patients and 84% when combined with H2 antihistamines. Hydroxy zine alone showed excellent to fair response in 60% patients and 72% when combined with H2 antihistamines.

There are differences in potency as measured by their ability to suppress a histamine-induced wheal and flare response (levocetirizine > fexofenadine). Levocetrizine is better than fexofenadine in suppressing histamine induced wheal and flare response (Grant JA, Howarth PH.et al)[9]

A recent trial compared the efficacy of levocetirizine with fexofenadine. Levocetrizine seems to have therapeutic advantage over fexofenadine in the treatment of CIU (Handa S, Dogra S et al).[10]

A study by Mann et al corroborates the finding that different newer-generation antihistamines have the potential to cause sedation, with fexofenadine being the least likely. This prescription-event monitoring study showed that the odds ratios for the incidence of sedation were 0.63 for fexofenadine and 5.53 for levocetirizine.[11]

Tashiro et al showed that fexofenadine did not occupy H1 receptors in the cerebral cortex, while levocetirizine occupied between 20% to 50% of the H1 receptors, depending on the brain region. These findings support evidence from comparative trials that indicate that although levocetirizine is less sedating than older antihistamines, it causes more sedation and impairment of performance than other second generation antihistamines.[12]

Iwabuchi, Tashiro M et al[12] study employed a variety of tests to examine their relative sensitivity and to establish the sedative profiles of three antihistamines – hydroxyzine, levocetirizine, and fexofenadine – compared with placebo. The results of the Stanford Sleepiness Scale SSS suggest a trend in increasing sleepiness: Fexofenadine=placebo< Levocetrizine< Hydroxyzine.

My study shows that sedation is the commonest side effect in Hydroxizine treated patients 37(74%) out of 50 patients. Dry mouth was reported in 13 patients (26%), Headache was reported in 3 (6%) and Constipation was complained in 8(16%) (Table 17).

In Group B (levocetrizine group) Sedation was 12(24%), dry mouth was 32(6%) and Constipation was 2(4%) in patients.

In Fexofenadine group, sedation 2(4%). Headache 12(2%) and no patients complained about dry mouth and constipation in this group.

So, side effects are more common in hydroxyzine group and fexofenadine has least side effect.

The increasing order of sedation with the various antihist amines was; first generation antihistamines> cetirizine> fexofenadine (Vivek K. David).[13]

Results of this study are comparable to the results obtained by various authors. It is more or less same as the results obtained by various authors.

Present study shows that Levocetrizine is better than fexofenadine and fexofenadine is more effective than Hydroxyzine.

5. Conclusion

Chronic Urticaria is a very common skin disease. The study focuses on various aetiological and pathological factors responsible for Chronic Urticaria.

Chronic Urticaria was found to be more common in females than males. It was found more in 25-34 year age group.

Maximum number of patients presented with the duration of disease of 12 months.

Finding suggest association of cyst of Amoeba and Giardia in some cases. Raised serum TSH and IgE level was seen in some cases. Non veg diet especially fish was associated with Chronic Urticaria.

Antihistamines are the most effective and preferred drug for the treatment of Chronic Urticaria.Traditional antihistaminic (hydroxyzine) and second generation antihistamines (levocetrizine and fexofenadine) was prescribed in therapeutic dosages and there results were interpreted.

Levocetrizine was found to be more effective than hydroxyzine and fexofenadine.

Fexofenadine was clinically superior than hydroxyzine in the treatment of Chronic Urticaria.Combination of H1 and H2 antihistamines was found to be more effective than H1 antihistamine alone.

Combination of Levocetrizine with Ranitidine was found clinically superior to the combination of fexofenadine and Ranitidine. Combination of Hydroxyzine and Ranitidine was less effective than above mentioned combination. Hydroxyzine was found to be the most sedative antihistamine. Fexofenadine was the least sedative and Levocetrizine was less sedative than Hydroxyzine but more than fexofenadine.

Side effects were (dry mouth, constipation) seen mostly in Hydroxyzine, less in Levocetrizine and least in Fexofenadine.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Rashmi Rani Assistant Professor

Dharmendra Kumar Associate Professor

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