ORIGINAL RESEARCH PAPER

Volume-9 | Issue-4 | April-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY TO EVALUATE EFFICACY OF SECOND GENERATION H1 ANTAGONIST MONOTHERAPY COMPARED TO ITS COMBINATION WITH H2 BLOCKER AND LEUKOTRIENE ANTAGONIST IN PATIENTS OF CHRONIC SPONTANEOUS URTICARIA.

Dermatology

Dr Suryash Jain* PG(Final year), Department of Dermatology, (TMMC&RC Moradabad) *Corresponding Author

Dr Sanath Aithal Professor and Head, Department of Dermatology, (TMMC&RC Moradabad)

ABSTRACT

BACKGROUND- One fifth of individuals in their life experience symptoms of urtcaria.Its multifactorial etiology makes it difficult to treat .Various combinations and regimens have been used in order to determine a more effective therapy.

METHOD-Ninety patients were randomly divided into three groups of 30 each

Group A patients were given Levocetirizine .

Group B - Levocetirizine with Ranitidine.

Group C –Levocetirizine with Montelukast .

RESULT- at the end of 4 weeks

- Montelukast in combination of levocetirizine showed a much better response which was demonstrated by a significant reduction in mean UAS7 throughout each visit.
- >75 percent reduction of score from baseline was seen in 56.7% of patient who received levocetirizine with montelukast which was higher than other two groups.(p-0.001)

KEYWORDS

INTRODUCTION

Urticaria is one of the commonest cutaneous conditions with high global prevalence which occur in fifteen to twenty percentage of individual affecting their quality of life [1].

Word "Urticaria" derived from a Latin word "Urtica" (nettle) due to its similarity to the lesion induced by nettle. Urticaria is described as a well-circumscribed, evanescent, erythematous dermal swelling of varying diameter which is extremely pruritic and which may or may not be associated with angioedema.[2] Wheals are short lived and disappear within thirty minutes to twenty four hours. Chronic spontaneous urticaria is defined as occurrence of wheal with or without angioedema for more than six weeks without any known stimulus[3].

The multifactorial etiopathogenesis makes the management of chronic urticaria a challenging job. As per current guidelines non-sedating second generation H1 anti histamine is main stay of management.

Non-sedating antihistamines target only single receptor which may not work in all cases. Addition of H2 antihistamine eg Ranitidine or LRTA(Monteleukast) may be a better alternative. Combination of anti H1and anti H2 acts via CYP3A4 increasing plasma concentration and potentiating each other. Acknowledging this we have compared the role of add on therapies in cases of chronic spontaneous urticaria Urticaria activity score a simple and validated tool is used to asses disease activity [4]. It is a self-assessment method carried out by patient on a daily basis.

Materials and methods

This was a randomized comparative clinical study including ninety patients with chronic spontaneous urticaria who were divided randomly in three groups visiting the Department of Dermatology, Venereology & Leprosy of Teerthanker Mahaveer Medical College, Moradabad (UP) .

INCLUSION CRITERIA

1. Newly diagnosed patient of chronic urticaria
2. Voluntary participation in the study
3. Patients aged 18 years and above of either gender were included in the study

EXCLUSION CRITERIA

1. Patient not willing to participate
2. Patient who were pregnant or lactating .

STUDY PLAN

- Patients fulfilling the inclusion criteria and giving informed consent were included in the study. A detailed clinical history, including history of the past illness, drug intake and co-morbidities was recorded. Urticaria activity score7 was assessed. Patients were randomly divided into three groups of thirty each.
- In study Group A individuals were given second generation antihistamine- Levocetirizine 5mg once daily dose.
- In study Group B individuals were given combination of H1 and H2 antagonist – Levocetirizine 5mg once daily dose with Ranitidine 150 mg twice daily dose.
- In study Group C individuals were given combination of H1 and leukotriene antagonist – Levocetirizine 5mg once daily dose with Montelukast 10 mg once daily dose.
- All the patients and their relatives were counseled about periodic follow-ups.
- Follow up was done after two weeks for four weeks to asses urticaria activity score7 and absolute eosinophilic count on an outpatient basis.

STATISTICALANALYSIS:

Data was recorded on a predesigned pro-forma and managed on an excel spread sheet. Appropriate statistical software was used for statistical analysis of the data collected.

RESULTS

90 patients with chronic spontaneous urticaria were selected and randomly divided in three groups of 30 each ,group A received only levocetirizine , group B -Levocetirizine with Ranitidine and Group C - Levocetirizine with Montelukast. Patient's response to therapy was followed at every visit.

Out of ninety patients male(49) were more than female(41) .

The mean age group of patients ranged between 30-35 years.

Majority of patients had onset of symptoms for more than six weeks to three months.

Dermographism was elicited in 36.7% patients.

Angioedema was present in 7.8% patients.

All three group exhibited insignificant reduction in TLC.

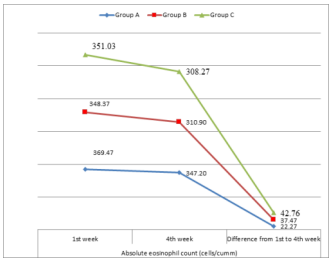
At the end of treatment there was drop in the levels of ESR in all three groups which was more marked in group B and group C(p-value-0.001 after 4 weeks and p-0.001 for total reduction)

Table1

Absolute Eosinophil Count (cells/cumm)		Mean	Std. Deviation	F-value	p-value	Post-hoc comparisons
1st week	Group A	369.47	85.80	0.129	0.880	N/A
	Group B	348.37	56.06			
	Group C	351.03	131.72			

4th week	Group A	347.20	77.82	4.337	0.016*	C,B > A
	Group B	310.90	66.65			
	Group C	308.27	108.55			
Difference from 1st to 4th week	Group A	22.27	36.15	16.907	0.001*	C,B > A
	Group B	37.47	32.49			
	Group C	42.76	43.70			

The change in Absolute eosinophil count was significantly more among group B and group C compared to group A. (p-value-0.016 at the end of treatment and p-0.001 for reduction from baseline)



Graph for Table 1

Table 2

Urticaria Activity Score		Mean	Std. Deviation	F-value	p-value	Post-hoc comparisons
1st week	Group A	20.57	2.45	0.292	0.747	N/A
	Group B	22.03	2.62			
	Group C	22.37	2.40			
2nd week	Group A	16.67	2.68	2.340	0.215	N/A
	Group B	16.70	3.21			
	Group C	15.93	2.78			
3rd week	Group A	13.60	2.75	10.470	0.001*	C, B > A
	Group B	11.87	4.34			
	Group C	9.87	3.57			
4th week	Group A	10.43	3.45	18.009	0.001*	C, B > A
	Group B	7.01	5.07			
	Group C	5.80	3.06			

The mean Urticaria severity score at 1st, 2nd, 3rd and 4th week was compared between group A, group B and group C using the One-way ANOVA test.The mean Urticaria severity score was reduced in all the groups with groups B and C showing more reduction than group A.Group C showed best response.

graph is blurred

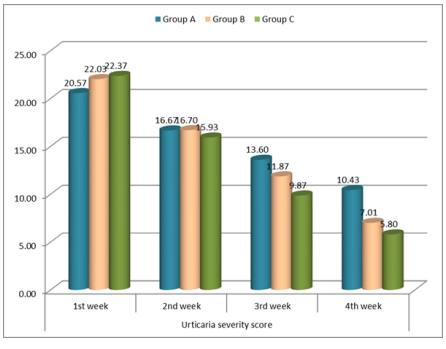
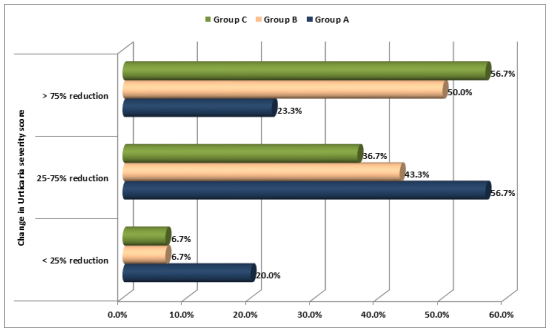


Table 3

Change in Urticaria severity score	Group A	Group B	Group C	Total
< 25% reduction	6	2	2	10
	20.0%	6.7%	6.7%	11.1%
25-75% reduction	17	13	11	41
	56.7%	43.3%	36.7%	45.5%
> 75% reduction	7	15	17	39
	23.3%	50.0%	56.7%	43.3%
Total	30	30	30	90

On statistical comparison the change in Urticaria severity > 75% was found to be significantly more among group B and C as compared to group A. Group C has maximum number of patients with >75% reduction.



Graph for Table 3

DISCUSSION

Urticaria is a routinely encountered affliction. It is difficult to diagnose and treat due to its heterogeneity. Multiple treatment modalities have been tried taking into account the diverse etiopathogenesis.There are different guideline for management of chronic urticaria put forward by various dermatological associations across the world. In all the guidelines second generation H1 antihistamines is the back bone of therapy.

The pathology of urticaria is complex. Different mechanisms have been described in its pathogenesis. Mast cells are the main cell affected. Activation of mast cell, basophil and degranulation is the key process in pathophysiology of urticaria which release histamine and inflammatory mediators. Human blood vessel poses both H1 (85%) and H2 receptors (15%) [5]. H1 receptor stimulation induces redness wheal and flare with smooth muscle contraction whereas H2 receptor is involved in erythema and wheal only [6].

Inflammatory mediators LTC4 LTB4 PGD2 leads to vasodilation, change in vascular permeability and smooth muscle contraction similar to histamine. Leukotriene D4 causes wheal and flare. [7] Leukotriene antagonist acts by blocking leukotriene D4 on the CysLT1 a cystenyl leukotriene receptor.

In our study we found significant difference in Absolute eosinophil count (cells/mm3) from 1st to 4th week among group B and group C compared to group A (C>B>A) with a p-value of 0.001. Anuradha et al[8] also reported 27.89 percentage reduction in AEC with levocetirizine.

The mean Urticaria severity score was reduced in all the groups with groups B(levocetirizine with)Ranitidine and C (levocetirizine with montelukast) showing more reduction than group A(levocetirizine), with group C showing better results than B (C>B>A)p-0.001.

Reduction in the score was appreciated in all groups after four weeks with mean score group A was 10.43, group B-7.01 and group C -5.80. A study conducted by Wan[9] also concurred that combination therapy showed significant improvement in UAS7 ($p < 0.05$) .Sweetlin et al[10] reported similar outcome.

Group C patients who were given Levocetirizine and montelukast together had higher regression in their symptoms which was inferred by significant reduction in change in Urticaria activity score with>75% reduction (56.6% patients) compared to Levocetirizine with Ranitidine and only Levocetirizine .

No significant adverse effects were noted in the three goups. Sedation was found in 4 patients each in group A and B and 2 patients in group C. 2 patients of group A and only 1 patient each of group B & C experienced Dizziness. However Headache was found in 1 patient of group A.

CONCLUSION

- In our study there was improvement in UAS scores in all groups over four treatment weeks.
- During all follow ups, the scores in both the combination group of levocetirizine and ranitidine and levocetirizine with montelukast decreased from baseline significantly ($P < 0.001$) (C>B) than Levocetirizine monotherapy
- Considering the significant results of all parameters it is evident that therapy targeting multiple receptors simultaneously gives a

much better response. In present study adjuvant use of second generation H1 antihistamine and leukotriene receptor antagonist showed better response.

- Hence we conclude that combination therapy consisting of Montelukast and levocetirizine is found to have higher efficacy and safety than Ranitidine and levocetirizine and levocetirizine alone.

FURTHER RECOMENDATION

The sample size in our study was of ninety patients and scores were assessed on the basis of treatment given over four weeks. More studies from different parts of the country with a larger sample size and longer duration along with assessment of impact on quality of life may give a better insight to the long term efficacy and tolerability of the therapeutic regimens.

REFERENCES

1. Maurer M, Abuzakouk M, Berard F, et al. The burden of chronic spontaneous urticaria is substantial: real-world evidence from ASSURE-CSU. Allergy 2017;72:2005-2016.
2. Deacock SJ.An approach to the patient with urticaria .Clin Exp Immunol. 2008; 153(2):151-161
3. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2) LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria: the 2017 revision and update. Allergy. 2018;73:1393–1414
4. Hawro T, Ohanyan T, Schoepke N, et al. Comparison and interpretability of the available urticaria activity scores. Allergy 2017;73:251-255
5. Harvey RP, Schocket AL9. . The effect of H1 and H2 blockade on cutaneous histamine response in man. J Allergy Clin Immunol 1980;65:136-9.
6. Babe KS, Serafin WE. Histamine, bradykinin and their antagonists. In: Hardman JG, Limbird LE, editors. The Pharmacological basis of therapeutics. 9th ed. New York: McGraw-Hill; 1996. p. 581-600.
7. Scadding, G.W.; Scadding, G.K. Recent advances in antileukotriene therapy. Curr. Opin. Allergy Clin. Immunol., 2010, 10, 370-376.
8. Anuradha P, Maiti R, Jyothirmai J, Mujeebuddin O, Anuradha M. Loratadine versus levocetirizine in chronic idiopathic urticaria: A comparative study of efficacy and safety. Indian J Pharmacol 2010;42:12-6.
9. Wan KS. Efficacy of leukotriene receptor antagonist with an anti-H1 receptor antagonist for treatment of chronic idiopathic urticaria. J Dermatolog Treat.2009;20(4):194-7.
10. S Sweetlin, Dinesh S. Efficacy of Montelukast and Ranitidine as an Add on Therapy for Chronic Urticaria. Int J Clin Pharmacol Toxicol. 2018;7(1):290-295.