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FEXOFENADINE HYDROCHLORIDE IN THE MANAGEMENT OF CHRONIC IDIOPATHIC URTICARIA (CIU) PATIENTS IN KARACHI

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ABSTRACT

Objective: To describe the effects of Fexofenadine HC1180 mg administered once daily for two weeks in patients in Karachi suffering from Chronic idiopathic Urticaria (CIU). **Design:** Open, non-comparative study conducted at PNSRahat (Naval Hospital) Karachi. Fexofenadine HC1180 mg once daily was prescribed for a two weeks period to patients aged 12 years and above with history of six or more weeks of idiopathic urticaria. Clinical symptoms and signs were evaluated before treatment and two weeks following treatment with Fexofenadine HCI. **Results:** 66 Patients completed a two weeks treatment period. 94 % patients reported reduction in severity of itching whereas 53% reported complete relief from itching. There was reduction in the number of wheals in 91 % of patients with complete disappearance of wheals in 54.5% patients. Erythema was present in 97% patients before treatment but was not detectable in 62% patients following treatment. While 63/66 (95%) patients complained that the condition interfered with their normal daily activity prior to treatment; after two weeks treatment with Fexofenadine HCI (53/66) 80% responded that it no longer interfered with normal activity. There was a statistically significant reduction in the mean Total Symptom Score from 13.3 (± 5.2) to 3.1 (± 3.5) with mean reduction of 10.2 (95% CI, 8.9-11.4). 15 (23%) patients reported a single side effect each, the most common being fatigue (eight), headache (six), and nausea (three). **Conclusion:** This study suggests that Fexofenadine HCI is effective and safe in relieving symptoms and signs of patients suffering from Chronic Idiopathic Urticaria.

Key Words: Chronic urticaria, H, antihistamines, Fexofenadine Hcl

INTRODUCTION

Urticaria is an extremely common problem affecting 15 and 20% of the population at some time in their lives[1]. Statistics in industrialized countries show that 1.4 % of the population visit their General Practitioner each year with urticaria[2].

Urticaria is a non-specific disseminated skin rash that appears as multiple short-lived itchy wheals. These vary greatly in shape, from blotchy red spots to annular (ring - shaped) lesions and in size from 1-2 mm to several centimeters in diameter[3]. The common feature of the urticaria rash is the transient nature of the wheals: while the condition itself may continue for days or even weeks or months[4,5].

Urticaria is rarely life threatening, but it can be extremely distressing for the patients. Itching is usually the most troublesome aspect and can be so intense as to severely disrupt sleep, thus impairing performance at work. Not knowing the cause of the condition, as in chronic idiopathic urticaria (CIU) can also seriously reduce patient's quality of life. Urticaria persists for more than six weeks, it is known as chronic urticaria. Chronic urticaria has no identifiable cause. Around 70% of all urticaria patients, acute and chronic, are eventually classified under this heading[5].

The treatment of patients with chronic urticaria presents a significant challenge to most experienced physicians. In urticaria, H_1 receptor antagonists are the corner stone

of symptomatic treatment. They act primarily by producing blockade of H_1 receptors on the sensory nerves and post capillary venules of the skin, thus relieving itching, wheeling and flaring. Fexofenadine HCl is a non-sedating anti-histamine with highly selective peripheral histamine H_1 receptor antagonist activity. It is recommended for relief of symptoms associated with CIU. Following oral administration, Fexofenadine HCl is rapidly absorbed and reaches maximum concentration within 1-2 hours and is sustained over a period of 24 hours.

OBJECTIVE

To describe the effects of Fexofenadine HCl 180 mg administered once daily for two weeks in patients suffering from Chronic Idiopathic Urticaria (CIU) in Karachi.

MATERIAL & METHODS

This was open, non-comparative study conducted at PNS Rahat (Naval Hospital) Karachi between March and September 1999. Patients of either sex, aged more than 12 years and with a history of CIU for six or more weeks were included in the study. Expectant and nursing mothers and patients with known hypersensitivity to any of the ingredients of Fexofenadine HCl were not eligible to participate. Each patient diagnosed with CIU was prescribed Fexofenadine HCl (Hoechst Marion Roussel) 180mg once daily for a period of two weeks.

In Study was completed a standard Clinical Record Form designed to gather specific information. This included patient's age, sex, severity of pruritis and the degree of interference with normal daily activity. Clinical findings were also documented on parameters such as number and size of wheals, intensity of erythema, extent of rash over the body, overall severity from the preceding two weeks. Possible variations in each of these parameters were categorized and assigned a numerical score (Table-I). The sum of scores for each of the parameter is henceforth referred to as the Total Symptom Score (TSS). The maximum possible score was 22.

To assess the efficacy of Fexofenadine HCl 180 mg daily, clinical information was documented at patient's first consultation and after a two weeks period during which the patient was on Fexofenadine HCl. It was planned to document any adverse event reported during treatment with Fexofenadine HCl and impression about the over-all efficacy and safety profile of Fexofenadine HCl at the end of the two week period was also recorded.

Descriptive statistics were generated to determine the change in number and proportion of patients before and after treatment for the parameters documented in Table 1. Paired t-test was conducted to report changes in mean total scores for each parameters before and after treatment with Fexofenadine HC1180 mg once daily for two weeks and 95% Confidence Intervals to report the difference in these mean scores.

RESULTS

Of 80 patients enrolled for the study, 66 (82.5%) successfully completed the two weeks study period by returning for the two weeks follow-up visits. Fourteen patients did not turn up follow-up. Data obtained from these 66 patients formed the basis of analysis being reported. There were 43 male and 23 female patients. The mean age was 32.9 (± 11.3) years.

All patients reported some degree of itching on their initial visit (Table-I). Fourteen (21.2%) patients reported itching characterized as minor irritation that was not annoying or troublesome (mild pruritis), 24 (36.4%) had itching that was annoying (moderate), 14 (21.2%) had very annoying itching (severe) and 14 (21.2%) had very intense (severe pruritis). After two weeks of taking Fexofenadine HC1180 mg once a day, 63 (95.4%) patients reported reduction in severity of itching; 35 patients (53%) reported complete relief from itching, 42.4% (28 patients) had mild itching and none had very severe itching.

Table-I. Changes in Clinical Parameters of Patients with CIU before and after treatment with Fexofenadine.

Score	Parameters	Before treatment N=66	%age	After treatment N=66	%age
	INTENSITY OF PURITIS				
0	None (no itchy patch)	00	0	35	53.0
1	Mild (minor irritation hardly noticeable or troublesome)	14	21.2	28	42.4
2	Moderate (ennoying & troublesome; may have interfered some what with normal daily activity and or sleep)	24	36.4	02	3.0
3	Severe (very annoying & troublesome; subsequently interfered with normal daily activity and or sleep)	14	21.2	01	1.5
4	Very severe (warranted a visit to a 14 physician)	14	21.2	00	0
	NUMBER OF WHEALS				
0	None	00	0	36	54.5
1	1-5	13	19.7	24	36.4
2	6-15	22	33.3	04	6.1
3	16-25	16	24.2	00	0
4	>25	15	22.7	02	3.0
	DIAMETER OF WHEAL (average)				
0	Absent	00	0	36	54.5
1	Small (<0.5cm)	21	31.8	22	33.3
2	Medium (0.25cm to 2.0cm)	17	25.8	08	12.1
3	Large (>2.0cm)	11	16.7	00	0
4	Giant (>4.0cm)	17	25.8	00	0
	INTENSITY OF ERYTHEMA				
0	Erythema Absent	02	3.0	41	62.1
1	Slight/Pale	15	22.7	23	34.8
2	Definite/Red	36	54.5	02	3.0
3	Extreme/Bright Red	13	19.7	00	0
	SKIN INVOLVEMENT				
0	None	00	0	32	48.4
1	Slight (32-50% of body involved)	16	24.2	29	43.9
2	Moderate (11-30% of body involved)	20	30.3	03	4.5

3	Severe (30-50% of body involved)	14	21.2	01	1.5
4	Very severe (>50% of body involved)	16	24.2	01	1.5
	INTERFERENCE WITH NORMAL DAILY ACTIVITY				
0	None	03	4.5	53	80.3
1	Mild	27	40.9	11	16.6
2	Moderate	36	54.5	02	3.0

On initial clinical examination, more than one wheal was detected in all (100%) patients (Table 1). Thirteen (19.7%) patients had between 1-5 wheals. Most patients (22/66) had between 6-15 wheals (33.3%) whereas 16 (24.2%). had between 16-25 wheals and 15 (22.7%) had more than 25 wheals. After treatment with Fexofenadine HC1180 mg once a day, there was complete clearing of wheals in 36 (54.5%) patients. A reduction in the number of wheals was also found in 24 additional patients. Hence a total of 60 (90.9%) out of the 66 patients were reported to have absolute reduction in the number of wheals as compared to the initial visit.

Prior to the treatment, 28 patients had wheals larger than 2 cm diameter, which shrunk after treatment. No patients had wheals larger than 2 cm after treatment (Table-I). There was no wheal in 36 patients (54.5%) whereas in 22 patients (33.3%) wheals reduced to less than 0.5 cm and in only 8 patients (12.1%) wheals present were between 0.5 to 2 cm in diameter after treatment with Fexofenadine HC1180 mg once a day.

On initial examination intensity of erythema was characterized as slight (pale) in 15 (22.7%) patients, definite (red) in 36 (54.5%) and bright red in 13 (19.7%). After two weeks of treatment with Fexofenadine HCl, it was found that 41 (62.1%) patients had no erythema, 23 (34.8%) had slight erythema and only two had a definite (red) erythema. 63/66 (95.5%) patients were found to have a reduction in the intensity of their erythema.

Very severe skin involvement (> 50%) was observed in 16 patients (24.2%) and severe skin involvement (30-50%) in 14 (21.2%) patients (Table 1). Twenty (30.3%) patients had moderate skin involvement (11-30%) and 16 (24.2%) had slight skin involvement (1-10%). After two weeks of therapy with Fexofenadine HCl 180 mg daily, 32 of the 66 patients (48.5 %) had no skin involvement, and 29 (43.9%) had only slight skin involvement. Only four patients (6.1 %) had moderate to severe skin involvement (>30%). The extent of skin affected reduced in 63 (95.5%) patients. No improvement was observed in only three (4.5%) patients.

Of the 66 patients, 63 (95.5%) on their initial visit reported that the condition interfered with their daily normal activity. After two weeks on Fexofenadine HC1180 mg, 53 (80.3%) patients reported that the condition no longer interfered with their normal activity and only 13 (19.7%) reported some degree on interference with normal daily activity.

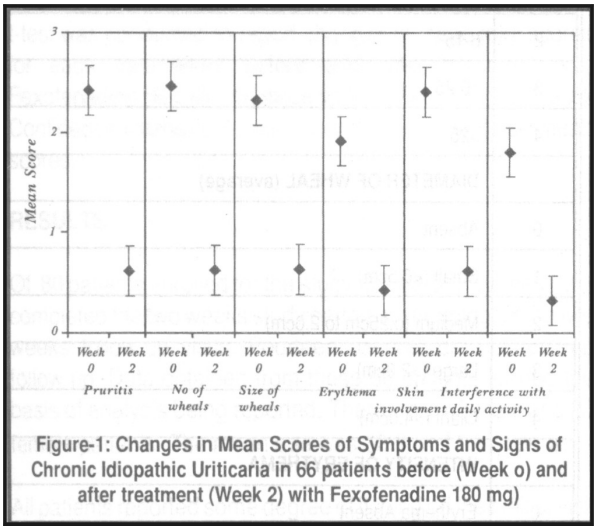

Figure-1: Changes in Mean Scores of Symptoms and Signs of Chronic Idiopathic Uriticaria in 66 patients before (Week o) and after treatment (Week 2) with Fexofenadine 180 mg)

There was a statistically significant reduction ($p<0.01$) in

the mean scores in all parameters observed when these scores were compared before and after treatment with Fexofenadine HC1180 mg once daily for two weeks (Figure-1). Using the paired t-test for analysis, the mean score for pruritis and wheals showed an almost similar reduction from 2.4 (±1.1) to 0.6 (± 0.9) (95% CI for difference in means, 1.6 -2.1). The mean score for the size of wheals showed a reduction from 2.3 (± 1.2) to 0.6 (± 0.7) (95% CI, for difference in means 1.5 - 2.0) There was a reduction in the mean score for arythema from 1.9 (± 0.8) to 0.4 (± 0.6) (95% CI for difference in means, 1.3-1.7) and for skin involvement from 2.4 (± 1.1) to 0.6 (± 0.8) (95% CI for difference in means, 1.6-2.1). Similarly there was a sharp reduction in the mean score for interference with normal daily activity from 1.8 (± 0.9) to 0.2 (± 0.5) (95% CI for difference in means, 1.3-1.7). The mean TSS also showed (Figure 2) a statistically significant reduction from 13.3 (±5.2) to 3.1 (±3.5) before and after treatment respectively with Fexofenadine HCI (95% CI for difference in means, 8.9-11.4).

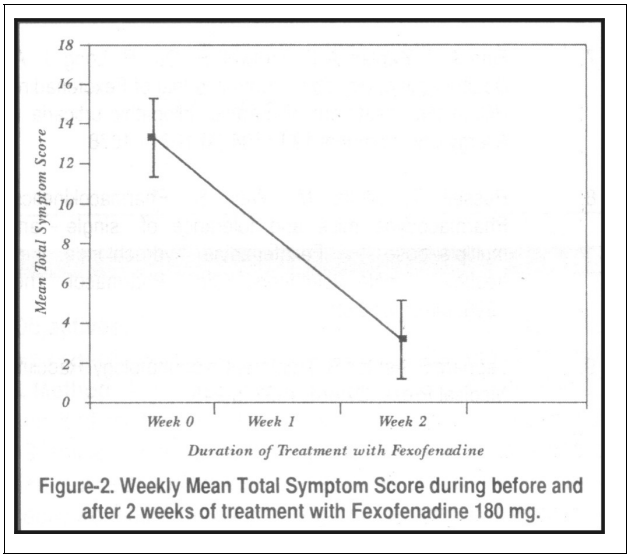

Figure-2. Weekly Mean Total Symptom Score during before and after 2 weeks of treatment with Fexofenadine 180 mg.

Fifteen (22.7%) patients reported one side effect each; and five (7.6%) reported more than one. The most common side effects reported were fatigue (eight patients), headache (six) and nausea (three). Two patients reported drowsiness and one severe backache. Of the five patients reporting more than one side effect, two patients reported headache and fatigue, one each reported fatigue and nausea, fatigue and drowsiness and headache with severe fatigue.

All except one episode of headache subsided in less than one week. Four of the eight patients reported fatigue of two weeks duration. Two had nausea of two weeks duration. None of the 66 patients discontinued treatment due to adverse events and neither did any of the patients report a serious adverse event during the course of treatment.

DISCUSSION

H_1 receptor antagonists are used in a variety of non-life threatening disorders such as CIU. In urticaria, H_1 receptor antagonists are the corner stone of symptomatic treatment. They act primarily by producing blockade of H_1 receptors on the sensory nerves and post capillary venules of the skin, thus relieving itching, whealing and flaring[6].

Results of our study demonstrate a clear trend in reduction of the signs and symptoms of CIU with the use of Fexofenadine HCI, a long acting anti-histamine. Fexofenadine HC1180 mg once daily in our patients has been found useful in reducing the number and size of wheals, intensity of erythema and extent of rash over the body (Figure 1). This also resulted in the reduction of overall severity and TSS from the preceding two weeks after completion of treatment with Fexofenadine HCI (Figure 2). Findings of our study are consistent with other clinical studies that demonstrate the effectiveness of 180 mg Fexofenadine HCI in the treatment of CIU[7]. A dose ranging study comparing Fexofenadine HCI and placebo also demonstrates that Fexofenadine HCI 180 mg once daily is highly effective for the treatment of CIU and provides significant relief from itching, number of wheals and reduces interference of CIU with sleep and normal daily activities[1]. Similarly another double-blind, placebo-controlled trial conducted to evaluate the safety and efficacy of Fexofenadine HCI in CIU concludes that the Fexofenadine HCI is superior to placebo in reducing signs and symptoms of CIU and is well tolerated[7].

Russell et al revealed that Fexofenadine HCI has a rapid onset of action with maximal inhibition occurring 1-2

hours after dosing[8]. Results from our study indicate that Fexofenadine HCI provides rapid improvement in the relief of symptoms and signs in cases of CIU.

In prescribing any medication, the risk benefit ratio of these agents must be carefully considered. The data reported from our study suggest that the risks associated with the use of Fexofenadine HCI are extremely low compared with the benefits likely to be achieved on treatment. The side-effects reported in our study are headache, nausea, dizziness and fatigue, which are common to non-sedating antihistamines[9]. These side effects were mostly singular and transient in duration. It is unlikely that patients who were lost to follow-up developed any serious adverse events. The benefits therefore offered by Fexofenadine HCI in reducing the troublesome aspect of itching and interference with normal daily activity reported by 95% patients to 20% of patients as indicated by our study overrides the minor side effects reported. Such benefits cannot be ignored in helping patients of CIU return to their productive routine work.

CONCLUSION

Urticaria is an extremely common problem affecting the individuals at some time in their lives. It is rarely life-threatening but extremely distressing and can also seriously reduce the patient's quality of life. Fexofenadine HCI provides rapid improvement in the relief of symptoms and signs and risks associated with its use are extremely low compared with the benefits likely to be achieved after treatment.

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