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ORIGINAL ARTICLE

Efficacy of Intramuscular Platelet Rich Plasma Versus Oral Antihistamine In Chronic Urticaria

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ABSTRACT

Background: Chronic urticaria is defined as a pruritic skin disorder that persists daily or about daily for >6 weeks. Chronic urticaria is a common problem in Pakistan. The common treatment method is oral histamine. Currently the important treatment method used is autologous serum therapy. The objective of this study was to determine the efficacy of intramuscular platelet rich plasma versus oral antihistamine in the treatment of chronic urticaria

Methodology: This study was randomized controlled clinical trial carried out at the Dermatology Department, Qazi Hussain Ahmad Complex Nowshera and alshifa clinic and skin aesthetic, Nowshera from May 2020 to May 2021. 100 patients were included in this research work. They were randomly divided into two groups of 50 patients each. One group was given autologous serum while the other was given antihistamine. The autologous serum group patients were treated by giving 9 intramuscular injection of autologous serum while the antihistamine group patients were treated with oral antihistamine on routine basis. UAS-7 (Urticaria Activity score-7) was used for measuring the effectiveness of both the treatment methods.

Results: At baseline in autologous serum group, the Urticaria activity score was 36.1 (±6.7) while in antihistamine group it was 35.2 (±5.4) respectively. At baseline Urticaria activity score was non-significant (p=0.85). At 4th week the mean Urticaria activity score in autologous serum group and antihistamine group was 18.3(±3.6) and 30.2.1 (±5.1) (p=0.01). At 9th week in autologous serum group, the Urticaria activity score was 11.3 (±6.3) while in antihistamine group it was 22.6 (±4.9). (p=0.04) At 12th week the mean Urticaria activity score in autologous serum group and antihistamine group was 7.1(±5.4) and 20.4 (±7.3) respectively (p=0.01).

Conclusion: Our study concludes that autologous serum therapy is more effective as compared to antihistamine in the treatment of chronic urticaria

Keywords: Chronic Urticaria; Intramuscular platelet rich plasma; Oral antihistamine.

INTRODUCTION

Chronic urticaria is defined as a pruritic skin disorder that that persists daily or about daily for >6 weeks [1]. The disease causing mechanism is not clearly known but majority of the studies consider autoimmunity as the most important contributing factor [2]. Due to leakage of plasma, transient skin or mucosal swelling occurs in urticaria leading to wheals and/or angioedema. Wheals are superficial skin swellings, while angioedema is a deeper swelling of the skin or mucosa. Angioedema is generally painful, not defined properly and does not change colour, while wheals are typically pruritic and pink or pale in the middle [3]. It has a considerable negative impact on the quality of patient's life [4]. Urticaria is thought to have a lifelong prevalence of 22.3 % with a point prevalence of roughly 1% [5]. The mean sickness time for this disease is 1-5 years [4]. Many infuriating factors such as type of diet, drug usage, alcohol intake, many viral infections and mental stress are important factors associated with the urticaria.

Numerous therapeutic options are available [6-8]. The treatment regimens for chronic urticaria include anti-inflammatory drugs, immuno-suppressants, antidepressants, antihistamines, antibiotics and monoclonal antibodies directed against immunoglobulin E [9-11]. In addition to these prescription drugs, mental distress avoiding, triggering risk factors identification, and cutaneous lotions use containing menthol and phenol can help to reduce symptoms of illness, but these are not concise treatments [12].

About 30-50 percent of chronic urticaria patients have circulating histamine-releasing auto-antibodies to the high-affinity IgE receptor FcεRIα on basophils or mast cells, or less often, antibodies to IgE [13]. In a subgroup of chronic urticaria patients, Hide et al. found that an intra-cutaneous injection of serum known as Autologous Serum Skin Test (ASST) causes an immediate hypersensitivity type skin response [14]. Auto-reactive group or autoimmune chronic urticaria is the name given to this category. These individuals are more likely to have a high itch or wheal score, as well as systemic symptoms and other autoimmune illnesses [15]. Autohemotherapy is considered as a significant and potentially curative treatment approach for ASST (Autologous serum skin test) positive chronic urticaria patients since circulating histamine releasing factors are accountable for the initiation of urticarial symptoms [16]. Bajaj et al. enhanced the approach by utilizing serum instead of whole blood since serum contains histamine releasing components [1]. The therapy became less painful as a result, and compliance improved. Patients with chronic urticaria have a significant antihistamine pill load and suffer from morbidity as a result of irritated symptoms. In autologous serum therapy, the patient own serum is injected intramuscularly on weekly basis. Even though exact mechanism of action is unknown, autologous serum treatment is thought to be able to desensitize auto-reactive chronic urticaria patients to the pro-inflammatory signals present in their blood [17]. It is easy, economical and potentially curative therapeutic option for chronic urticaria patients with no adverse effects [18]. The evidences for the positive effects of autologous serum therapy for the treatment of skin disorders, especially chronic urticaria are limited [19, 20]. Chronic urticaria is a common problem in Pakistan. The common treatment method is oral histamine. To our knowledge no study has been in Pakistan done on autologous serum therapy for treatment of chronic urticaria. This comparative controlled trial was therefore piloted to find-out the efficacy of autologous serum therapy and antihistamine oral pills in treating chronic urticaria patients with the hypothesis that autologous serum therapy will be effective than antihistamine oral pills in treating chronic urticaria patients.

Operational definition

Swelling: The swelling was considered as positive if the diameter of swelling caused by autologous serum was 1.5 mm more than physiologic saline while it was considered as negative if there was no reaction or only erythema after 60 minute [21].

Efficacy: It was defined as absence of urticarial wheals and pruritus after the treatment [22].

MATERIALS AND METHODS

This study was randomized controlled clinical trial conducted at the at the Dermatology Department, Qazi Hussain Ahmad Complex

Nowshera and alshifa clinic and skin aesthetic, Nowshera. The duration for this research study was one year from May 2020 to May 2021. Approval of the study was given by research and ethical committee of the hospital. From all the patients included in this study, a written consent form was signed. All the included patients were examined physically by expert dermatologist. With 80% power and 5% probability of type 1 error and 10% dropout, the calculated sample size was 100 [23].

Patients of any sex and 18-55 years age having chronic urticaria were enrolled for this study. Only those patients who gave written informed consent and were wiling for follow up were included in the study.

The criteria for exclusion in our study were patients having acute urticaria, problem of immune-suppression, any major organ problem, on steroid treatment, patients not agree to sign consent form, having age less than 18 years and unable to come weekly for follow up, alcohol addiction, lactating mothers and patients suffering from hepatitis B and C. These all were excluded because any of these factors might hinder the study's performance or raise the chances of a negative consequence.

Procedure, intervention and follow up: 27-gauge (10ml) sterile syringe was used and 5ml blood was taken from all the patients included in the autologous serum group. In the glass tubes the blood samples were placed without having anticoagulants. This blood was kept at room temperature for 30 minutes and then centrifuged at 3000rpm for 10 minutes. Both the forearms were cleaned and in the right forearm both the autologous serum (0.05ml) and negative control (0.05ml physiologic saline) were injected apart. While in the left forearm a positive control (0.05ml histamine) was injected to form papule for prevention of interference of swelling and erythemas. All the results were assessed after 30 minutes. The diameter of swelling was used to interpret the results. In this research work, a total of 100 patients were enrolled and were categorized into two groups. 50 patients were kept in autologous serum group and 50 patients were kept in antihistamine group. The autologous serum group patients were treated by injecting 9 intramuscular injection of autologous serum while the antihistamine group patients were treated with oral antihistamine. In the process of autologous serum therapy 5 ml of blood was taken from patient using sterile needle. The blood was then centrifuged for 10 minutes at 3000rpm. Then 2ml of the serum was taken in 27G needle and injected intra-muscularly into the gluteus muscle [1]. UAS-7 (Urticaria activity score-7) was used for measuring the effectiveness of both the treatment methods. The primary outcome measures for effectiveness were Urticaria activity score-7. UAS is commonly used for patients with chronic urticaria, which involves hives and pruritus severity. The UAS-7 was determined as the combination of pruritus severity and number of hives within 1 week prior to blood sample. Patients self-reported 24-hour self-evaluation ratings for seven days using the scheme similar to previous study [24].

Data Analysis: All the data was entered in SPSS software version 23. The values were calculated as means and standard deviation. Mann- Whitney U Test was used for comparing effectiveness of both the methods. A p value of <0.05 was considered as significant. All the results were presented in graphical and tabulated form.

RESULTS

There were 50 patients in autologous serum group and 50 patients in antihistamine group. In both the group there were more females than males. The mean age was comparable in both the groups. The mean age in autologous group was 31.4 (±4.2) years while in antihistamine group the mean age was 32.2 (±3.5) years. The duration of disease in both the group was almost same. In autologous serum group the mean duration of disease was 3.2 (±4.2) years ranging from 5 month to 8 years while in antihistamine group the mean disease duration was 3.3 (±5.0) years ranging from 6 month to 9 years. Urticaria activity score was comparable in both the group at baseline observation. We analyzed the average of UAS-7 during the weeks of therapy and follow-up to establish the success of the autologous serum injections, and we noticed a substantial drop in UAS-7 followed by a major improvement in urticarial symptoms at the 4th week than baseline, the 9th week than fourth week, and the 12th week compared than 9th week. By comparing the mean of UAS-7 over the weeks of treatment and follow-up in the antihistamine group, we observed no significant drop in UAS-7. (Table 1)

Table 1: Comparison of Urticaria activity score-7 in both the groups

Urticaria activity score-7	Autologous serum group	Antihistamine group	P value
Baseline	36.1 (±6.7)	35.2 (±5.4)	0.85
4th week	18.3(±3.6)	30.2.1 (±5.1)	0.01
9th week	11.3 (±6.3)	22.6 (±4.9)	0.04
12th week	7.1(±5.4)	20.4 (±7.3)	0.01

DISCUSSION

Chronic urticaria is a prominent disease that has a detrimental impact on both personal and professional lives because of its long-term annoyance and poor therapeutic approaches. The autologous serum skin test is an in vivo test that evaluates auto responsiveness in chronic urticaria patients, especially during active illness stages [25]. The treatment of urticaria is based on two main mechanisms: the first is to neutralize the impact of degranulation products, and the second is to inhibit degranulation. Antihistamines and leukotriene inhibitors are the most common treatments for urticaria; however they are not always enough. To treat urticaria symptoms, immunosuppressive medications such as cyclosporine, methotrexate, corticosteroids and adalimumab must be used, with the goal of blocking degranulation by antibody production [26]. Immunosuppressive drugs are circumscribed in their usage due to their more side-effect and heavy cost [7]. On the other hand autohemotherapy is considered as a significant and potentially curative treatment approach for ASST positive chronic urticaria patients since circulating histamine releasing factors are accountable for the initiation of urticarial symptoms [16]

In our study, 100 patients were included. There were 50 patients in autologous serum group and 50 patients in antihistamine group. In both the group there were more females than males. In autologous serum group, male were 15 (30%) and female were 35 (70%) while in antihistamine group there were 13 (26%) male and 37 (74%) female. Our results are in accordance with the reported study who revealed that chronic urticaria is one of the skin disorders with a strong female preponderance, with an overall female/male ratio of about 2-4:1[27]. Thyroid disorders, particularly autoimmune thyroid illnesses, have been linked to chronic urticaria. Thyroid diseases are significantly more frequent in women than in males, as is widely known [28]. Hypothyroidism was the most often identified thyroid illness in individuals with CU, observed in 9.8% of patients and 0.6 percent of the control group in a recently published research on 12,778 CU patients [29]. Females were more likely than men to be impacted by the combination of hypothyroidism and CU. The mean age was comparable in both the groups. Similar high numbers of female were reported with chronic urticaria in a previous study [1, 30]. The mean age in autologous group was 31.4 (±4.2) years while in antihistamine group the mean age was 32.2 (±3.5) years. A previous study done by Debberman et al. in 2014 reported similar ages to our study and reported no significant difference between the mean ages of both the group [31]. This might be because with ageing, the skin undergoes structural and physiological changes. Aging is connected with a loss in skin thickness as well as a decrease in cutaneous vascularity and cellularity. The number of cutaneous mast cells decreases as well [32].

The duration of disease in both the group was almost same. (Table 1) A previous study reported similar duration of the disease with no significant difference between the case group and control group [30]. Urticaria activity score was comparable in both the group at baseline observation (Table 1). We analyzed the average of

UAS-7 during the weeks of therapy and follow-up to establish the success of the autologous serum injections, and we noticed a substantial drop in UAS-7 followed by a major improvement in urticarial symptoms at the 4th week than baseline, the 9th week than fourth week, and the 12th week compared than 9th week. By comparing the mean of UAS-7 over the weeks of treatment and follow-up in the antihistamine group, we observed no significant drop in UAS-7. During all these observations p value was significant for autologous serum treatment. (Table 1) This research validates Patil et al. [17] findings that UAS-7 levels drop after a few weeks. This study supports the findings of Bajaj et al. [1], who reported that after nine weekly ASTs, about 60% of ASST positive patients exhibit a substantial improvement in their signs and symptoms. This research is also in line with Abdallah et al. [33] in Egypt, who revealed that AST are beneficial in managing urticarial symptoms in a substantial proportion of ASST-positive patients. As autologous serum therapy decreases urtcarial symptoms, it was proven to be an excellent treatment method. AST was generally tolerated, with just a few patients experiencing mild adverse effects such as redness, itching, and dizziness shortly after the initial injection. The limitation of our study was short duration of follow-up and small sample size. A multi-centre study based on large sample size with long term follow-up is needed to further validate the effectiveness of autologous serum therapy. To validate its effectiveness on symptom reduction in people with chronic urticaria, more investigation is necessary.

CONCLUSION

Our study concludes that autologous serum therapy is the effective method than antihistamine therapy for treatment of chronic urticaria. Although the actual mechanism by which autologous serum therapy works is unknown, it may prove to be a more economic and curative approach, reducing pill load, and showing promise in the treatment of chronic urticaria, independent of its autoimmune nature.

Recommendation: Our study suggest to perform a multi-centre study based on large sample size with long term follow-up to further validate the effectiveness of autologous serum therapy.

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