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CLINICAL EVALUATION OF HERBAL FORMULATION -VILVA ILAI KUDINEER FOR KANAKADI (URTICARIA) IN CHILDREN

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ABSTRACT

Siddha system is a vast and unique system which defines health as a prefect state of physical, psychological social and spiritual wellbeing of an individual. In siddha medicine there is not only cure of disease but it also improve the quality of life by prevention and rejunuvation. Urticatria is one of the most common skin disease, characterized by the development of wheals(hives), angioedema, or both and it is classified as acute or chronic form based on the duration of illness. Urticaria of longer than 6 weeks duration is classified as chronic urticaria, which is further classified into chronic spontaneous or inducible urticaria has a more significant impact on quality of life due to recurrence and unknown etiology. Siddha medicine is having many formulations to treat kanakadi (urticaria), one among them is Vilva Ilai Kudineer described in siddha literature. 10 children those were attending Kuzhanthai Maruthuvam OPD with the symptoms of Kanakadi (urticaria) were recruited for this pilot study. All patients were treated with Vilva Ilai Kudineer -30 ml for 48 days. All the 10 patients were subjected into Urticaria Activity Score(UAS-7) before(0^{th} day) and after treatment(48^{th} day). Results were observed by analyzing the USA-7 Assessment scale. The p value is highly significant($p<0.001$). so the treatment was significantly improving Kanakadi(Urticaria). From this pilot clinical study its observed that Vilva ilai kudineer is having good efficacy in the treatment Kanakadi (Urticaria). Vilva ilai kudineer is easily preparable and cost effective compared with conventional treatment for Kanakadi(Urticaria).

KEYWORDS: Siddha medicine is having many formulations to treat kanakadi (urticaria), one among them is Vilva Ilai Kudineer described in siddha literature.

INTRODUCTION

Urticaria is one of the most common skin disease, characterized by the development of wheals (hives), angioedema, or both and it is classified as acute or chronic form based on the duration of illness. Urticaria of longer than 6 weeks duration is classified as chronic urticaria, which is further classified into chronic spontaneous or inducible urticaria. Acute urticaria is more prevalent than chronic urticaria; however, chronic urticaria has a more significant impact on quality of life due to recurrence and unknown etiology.[1] As in adults, the causes are different between acute and chronic urticaria in children,[2,3,4,5,6,7,8] and it is difficult to determine the exact prevalence of childhood urticaria due to lack of papulation-based studies.

Common causes or triggers of acute urticaria in children include infections, medications, and foods, while acute spontaneous urticaria is common in young children with atopy. Infection appears to be a more frequent predisposing cause of urticaria in infants and children compared with adults. Infection is the most frequently documented cause (more than 40%) in children with acute urticaria.[1,2,3] In a recent systematic review, viral infection was a potential trigger and sometimes the main cause in acute and chronic urticaria.[4] The rate of identification of a specific cause in children with chronic urticaria varies from 20%-50%, but in practice, most patients have no precise causes and are classified as chronic idiopathic urticaria. The underlying causes of chronic spontaneous urticaria do not appear to be different between children and adults; however, their frequencies are different.[1] In recent studies, more than 30% of children with chronic urticaria are classified as chronic autoimmune urticaria.[5,6]

Nonsedating H_1-antihistamines are the current mainstay for initial treatment and are the only agents licensed for

use in patients with chronic idiopathic urticaria. However, a majority of patients do not have a response to H_1-antihistamines, even when the drugs are administered at three to four times their licensed dose.

Treatment options for patients who do not have a response to H_1-antihistamines include the use of H_2-antihistamines, leukotriene-receptor antagonists, systemic glucocorticoids, cyclosporine, hydroxychloroquine, dapsone, methotrexate, sulfasalazine, and intravenous immune globulin. None of these agents have yet received regulatory approval for the treatment of chronic idiopathic urticaria. In addition, the data supporting the use of these drugs are limited, and long-term use of some of the agents can be associated with substantial side effects.

In order to reduce those side effects, the present study will be conducted in vilva ilai kudineer for kanakadi(urticaria). Marmin or (7-(6',7'-dihydroxygeranyl-oxy)coumarin is an active compound isolated from Agele marmelos. Coumarin derivatives isolated from plants are considered potential to be developed as anti-allergic agents. Componds 3,4-dimethyl-7-[4-(p-chlorobenzyl)-pyperazine-1-yl]-propoxicoumarin dihydrochloride was reported topossess an activity as a histamine receptor antagonist. the compound also inhibited antigen-induced histamine release from sensitized human leucocytes and inhibited the re-uptake of histamine by isolated human leukocytes.[9] Majority of children with the sympotoms of urticaria are enrolling in Kuzhanthai Marudhuvam opd in NIS. the management and treatment with single herbal formulation vilva kudineer which has anti histaminic and anti inflammatory property and will be the safer drug for children.

SUBJECTS AND METHODS

This pilot study was conducted in opd of the Ayothidoss Pandithar Hospital, National Institute of Siddha, Tambaram Sanatorium, Chennai-47. The study was conducted in accordance with the good clinical practice guidelines of the Indian Council for Medical Research(ICMR-GCP) and was approved by the Institutional Ethics Committee. (IEC NO - NIS/IEC/2019/P-6).

SUBJECTS

10 children who were attending the OPD of Kuzhanthai maruthuvam (Pediatric OPD) for the treatment of Kanakadi (Urticaria) were the subjects for this study. All the 10 patients were screened as per the screening profoma and those meeting the inclusion criteria were included in this study. The patients were treated for 48 days and followed for 3 months including the treatment period. Subjects who were between the age group 5 -12 years, with the symptoms of acute and chronic urticaria with the symptoms of wheel formation, itching, erythymatous rashes, willing to give written consent and assent for this study were included. Children with the symptoms of Fever with rashes, Pitriasis rosea, Drug eruptions, Erythema multiforme, Other systemic illness and Acute bronchospasm were excluded from this study. Methods Standard operating procedure for preparation of trial drug. The Fresh leaves of Vilva ilai (*Agele marmoleos)* were collected and authenticated by Asst. professor of medicinal Botany of NIS, Chennai. The leaves were washed in running water and dried well. Dried leaves were grinded using pulvarizer in Gunapadam Laboratory of National Institute of Siddha, Chennai-47.

Table 1: Ingredients of Vilva ilai kudineer chooranam.

S.NO	TAMIL NAME	BOTANICAL NAME	ACTION
1	Vilvam	*Agele marmoleos*	Anti histamine, Anti inflamatory

The above ingredients were taken 5Kg after purification and roughly powdered in a stone mortar and the prepared drug was stored in a clean and dry air tight glass container.

Dispensing

The medicine was dispensed in ziplock cover with proper labeling during each visit for seven days.

Observation

Urticaria activity score (UAS-7) is considered to be the direct method of analysis for diagnosis and prognosis of the patient affected with Urticaria. This Score were assessed on day 0 and repeated on day 48 of the trial period. The primary efficacy outcome was efficacy of the trial drug is measured using urticaria activity scale and improvement in the clinical symptoms was assured.

Safety was assessed based on the adverse events recorded during the study. At the end of the study, the three-point Assessment Scale for Efficacy (Good, Moderate and Poor) was used to assess the efficacy results. If there is no wheal formation and no pruritis then it is stage 0, wheal formation is <20 wheals/24 hrs with mild pruritus it is mild stage 1, 20-50 wheals/24hrs with troublesome pruritus, but does not interfere with normal daily activity or sleep it is moderate stage 2,>50 wheals/24 hrs with severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep classified severe stage 3.If 2stages improved then it is considered as good improvent,1 stage improved it is considered as moderate improvement, if there symptoms are static or aggravated then it is considered as poor improvement. Compliance was assessed using the Kudineer Chooranam left in packets and those who consumed over 80% of Kudineer Chooranam were classified as compliant. I

Study enrollment

Children reporting at the Kuzhanthai maruthuvam OPD of the Ayothidoss Pandithar Hospital, National Institute of Siddha, Tambaram sanatorium, Chennai-47 with satisfying inclusion & exclusion criteria were selected for the study. The patients were informed about the study, trial drug, possible outcomes and the objectives of the study in their own language and terms understandable to them and the informed consent was obtained in the consent form. They were instructed to attend the OPD once in 7 days.

Inclusion Criteria

- Age group between 5 to 12 years.
- Both male and female children included.
- Acute and chronic urticaria
- Wheel formation
- Itching
- Erythymatous rashes.
- Those who are willing to sign in consent form.

Conduct of the study

The trial drug was given by the investigator in the OP department of Kuzhanthai Maruthuvam, NIS, Chennai. All the patients were asked to attend the OPD once in the 7 days. In every visit the clinical assessment was recorded in the prescribed case report form (CRF) individually. The UAS-7 Scale were assessed before and after treatment. At the end of the trial (48 days) the patients were advised to come for two more months for further follow-up.

OBSERVATION AND RESULTS

10 patients were recruited for this pilot study. All patients were treated with Vilva ilai Kudineer 30 ml twice a day. All patients were advised for dietary regimen as per Siddha philosophy.

All the 10 patient were assessed by using UAS-7 Scale after 48 days of treatment and the obtained results were tabulated below.

S.NO	OP NO	WHEALS		PRURITIS	
		BEFORE	AFTER	BEFORE	AFTER
1		2	1	3	2
2		2	0	2	0
3		3	3	3	3
4		2	1	3	2
5		2	1	3	1
6		3	1	3	1
7		2	0	2	0
8		1	0	1	0
9		3	3	2	2
10		2	1	2	0

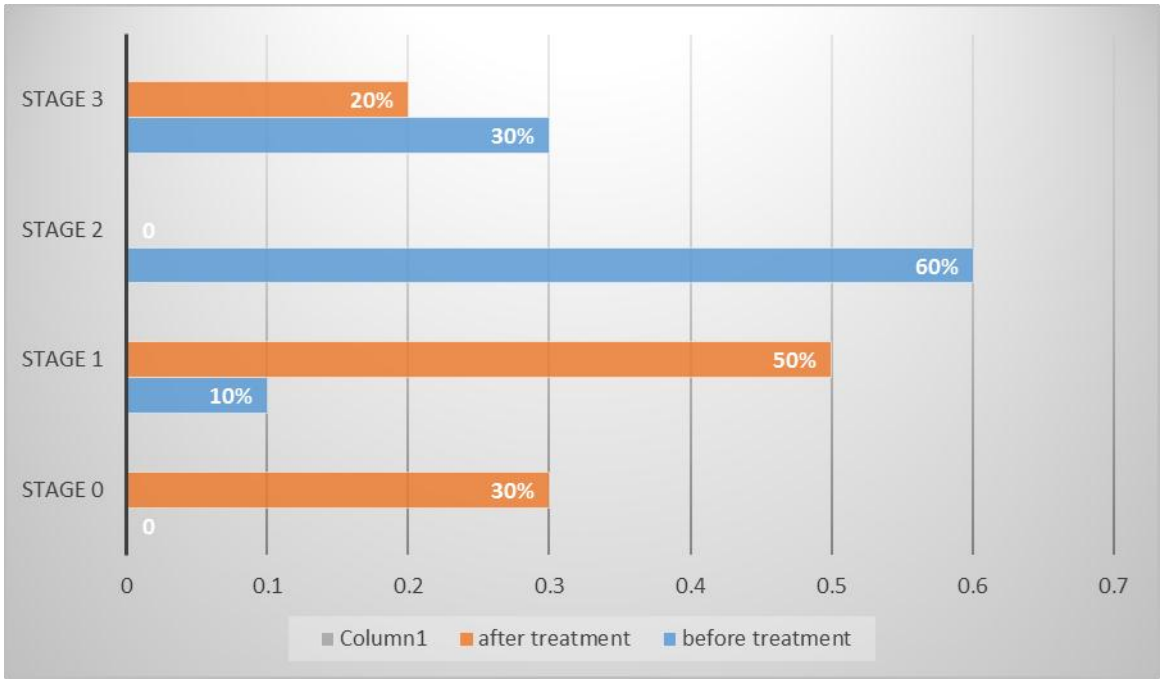

Fig 1: Wheal formation before and after treatment.

Before treatment 60% of sample were belong to stage 2, out of this 40%(stage 2 to stage 1) had moderate improvement, 20%(stage 2 to stage 0) had good improvement after treatment. Before treatment 30% of sample were belong to stage 3,out of this 10%(stage 3 to stage 1) had good improvement, 20% of sample symptoms were static had poor improvement after treatment. Before treatment 10% of sample belong to stage 1, out of this 10% (stage 1 to stage 0) had moderate improvement after treatment.

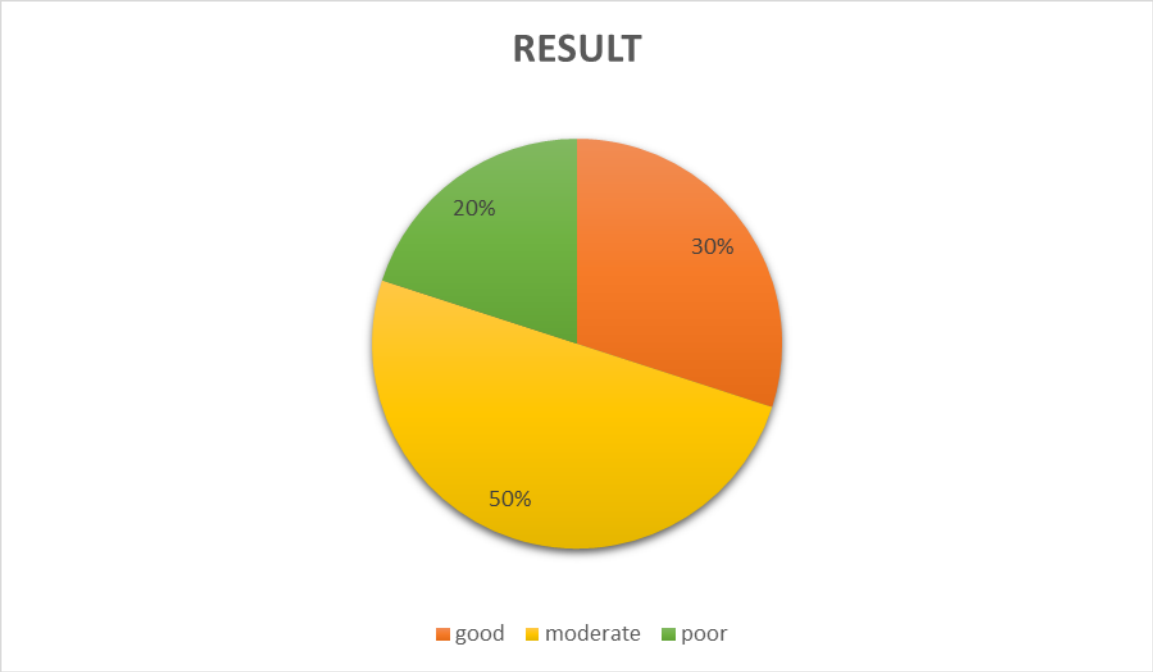

Fig 2: Result of efficacy of vilva ilai kudineer in wheal formation.

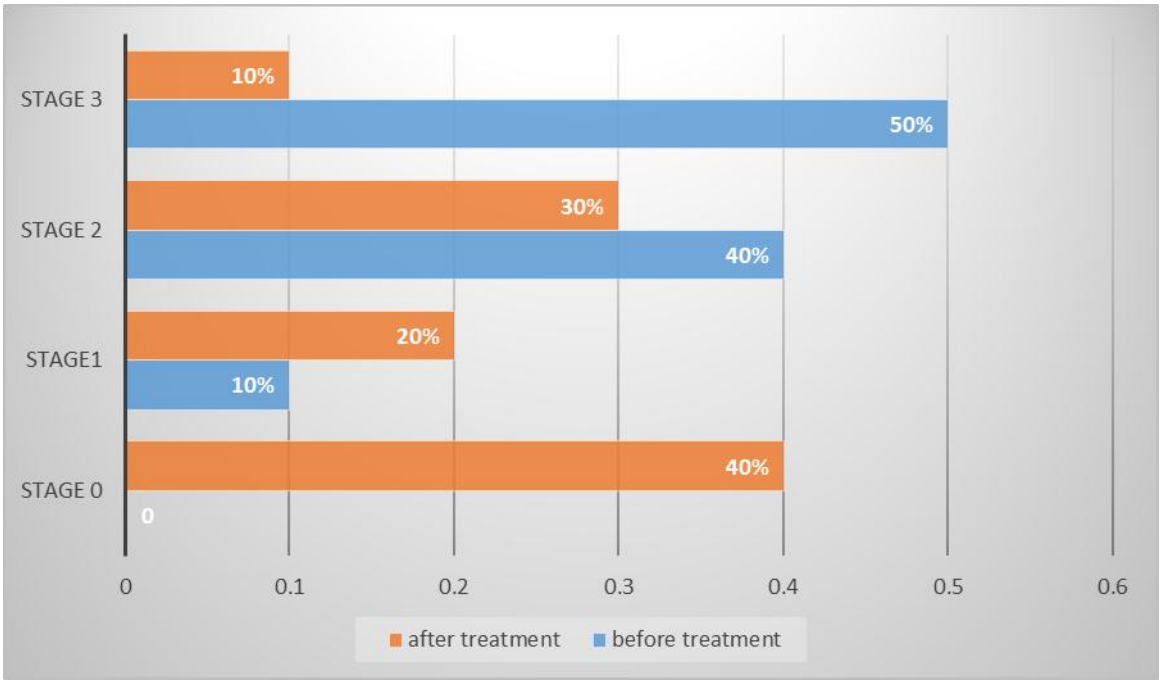

Fig 3: Pruritis formation before and after treatment.

Before treatment 50% of sample were belong to stage 3, out of this 20%(stage 3 to stage 2) moderate improvement, 20% (stage 3 to stage 1) good improvement, 10% of them symptoms were static poor improvement after treatment. Before treatment 40% of sample were belong to stage 2, out of this 30%(stage 2 to stage 0) good improvement, 10% of them symptoms were static poor improvement after treatment. Before treatment 10% of them belong to stage 1, out of this 10%(stage 1 to stage 0) moderate improvement.

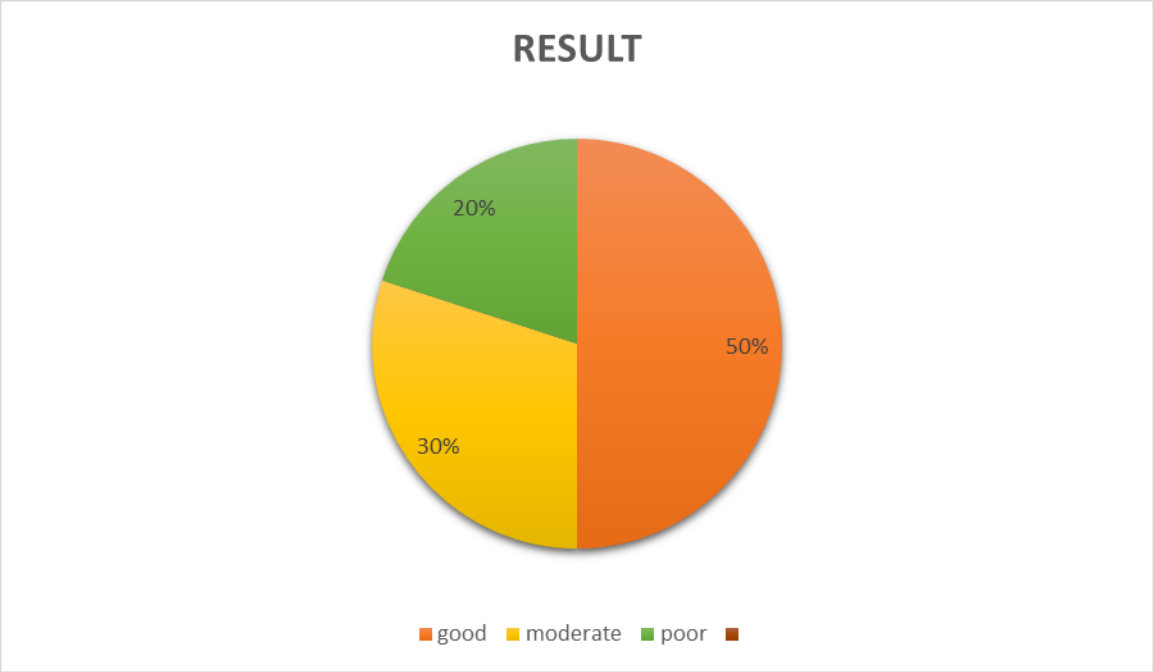

Fig 4: Result of efficacy of vilva ilai kudineer in pruritis.

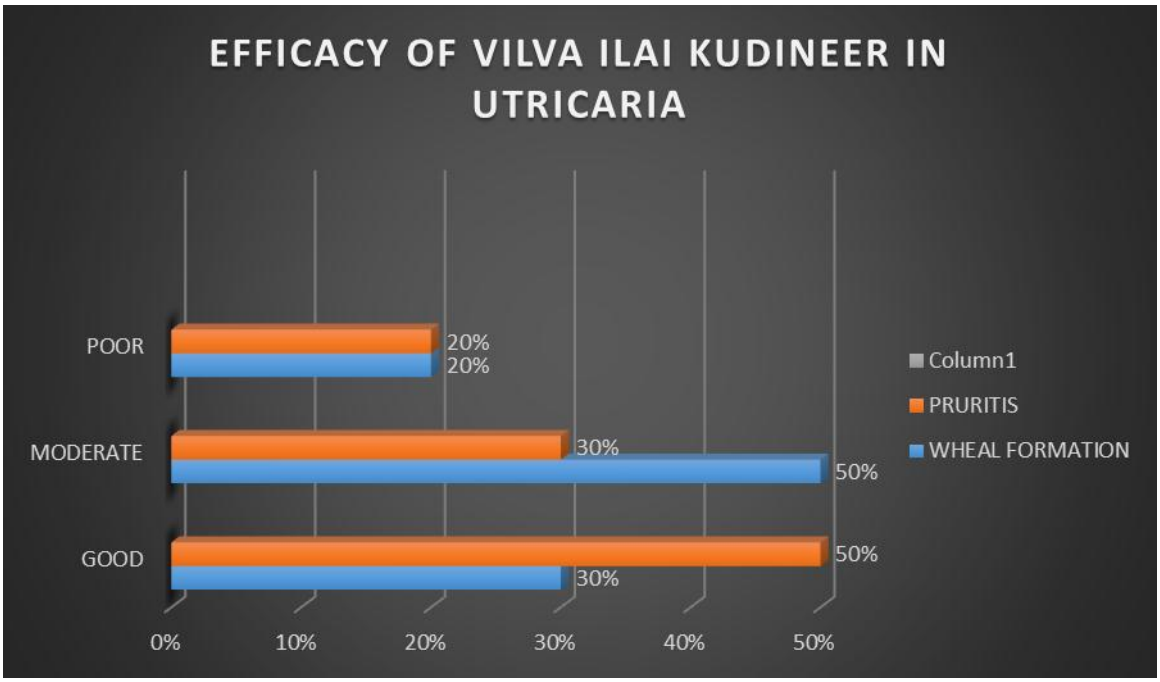

Fig 5: Efficacy of Vilva Ilai Kudineer In Urticaria.

DISCUSSION

Among skin diseases 30% to 40% of them belong to urticaria, since more number of patient are approaching kuzhanthai maruthuvam, OPD of the Ayothidoss Pandithar Hospital, National Institute of Siddha, Tambaram sanatorium, Chennai-47, so the author has decided to conduct this pilot study. The study was conducted in accordance with the good clinical practice guidelines in the Indian Council for Medical Research (ICMR-GCP) and was approved by the Institutional Ethics Committee **(**IEC NO - NIS/IEC/2019/P-6).

The trial drug vilva ilai kudineer was prepared as per standard operating procedure by following (GLP) Guidelines. After geeting informed consent 10 Patients were recruited for this pilot study those meeting the inclusion and exclusion criteria. All the patients were treated with vilva ilai kudineer 30 ml twice a day for 48 days. Before starting the trial assessment of urticaria were done using the scale Urticaria activity score (UAS-7). This Score were assessed on day 0 and repeated on day 48 of the trial period. The results were analysed by comparing the assessment scale before and after treatment.

The three-point Assessment Scale for Efficacy (Good, Moderate and Poor) was used to assess the efficacy results. In wheal formation 30% of them had good prognosis, 50% of them had moderate prognosis, 20% of them had poor prognosis. In pruritis 50% of them had good prognosis, 30% of them had moderate prognosis and 20% of them had poor prognosis. Vilva ilai kudineer shows more prognosis on wheal formation than pruritis. The p value is highly significant ($p<0.001$). So the treatment was significantly improving Kanakadi (Urticaria). From this pilot study there is no adverse reaction was reported during this entire study period.

CONCLUSION

From this pilot clinical study its observed that Vilva ilai kudineer is having good efficacy in the treatment Kanakadi (Urticaria). Vilva ilai kudineer is easily preparable and cost effective compared with conventional treatment for Kanakadi(Urticaria). So the author recommended that to conduct this trial in larger number of population for better exploration of this novel drug.

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