Research Article

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AN OPEN COMPARATIVE CLINICAL TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF SIDDHA DRUGS PANCHAMUGA CHENDHURAM AND KUNDAVAADHI THAILAM IN PSORIASIS

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ABSTRACT

Aim: The patients with psoriasis, like those with other major medical disorders, have reduced levels of employment and income as well as a decreased quality of life. The treatments such as methotrexate, cyclosporine have been used for many years, but the safety profile of this treatment is minimal. Hence an idea is created to conduct a clinical trial to assess the efficacy and safety of Siddha trial drugs "Panchamuga Chendhuram" (PMC) and "Kundavaadhi Thailam" (KVT) in the management of psoriasis. Materials and methods: 40 patients of either sex was divided into 2 groups. The Group I treated with *PMC* alone at 65mg dose twice daily, for 48 days. The Group II treated with both PMC and KVT. Efficacy was determined by a percentage reduction in Psoriasis Area and Severity Index (PASI) score. Safety of drug PMC was evaluated by measuring LFT and RFT. Results: PASI Score Mean and SEM (n) at 48th day after treatment with the trial drug PMC alone and with both PMC and KVT were 2.295 ± 0.531* (20), 5.305 ± 1.982* (20) respectively, and P value <0.001 is statistically significant. Safety parameters such as T. Bilirubin (P < 0.05), T. Protein (P = 0.361), SGPT (P = 0.798), SGOT (P < 0.05), ALP (P = 0.436), urea (P= 0.810), creatinine (P = 0.207), uric acid (P = 0.836) were also have no changes before and after treatment. Conclusion: Hence it is concluded that the drugs were effective and safe in psoriasis patients.

KEYWORDS: Psoriasis, Siddha drug, Chendhuram, Safety, Efficacy

INTRODUCTION

Psoriasis is a common, chronic, autoimmune disease that causes dry, red, scaly patches and flakes to appear on the skin. The reported prevalence of psoriasis in countries ranges between 0.09% and 11.4%, making psoriasis a serious global problem[1,2]. The main histopathological change of psoriasis is accelerated keratinocyte cell proliferation[3]. Although an early concept of the pathogenesis of psoriasis focused on the proliferation and differentiation of keratinocytes, recent studies have recognized that dysregulation of the immune system plays a critical role in the development of psoriasis. The interactions between dendritic cells, T cells, keratinocytes, neutrophils and the cytokines released from immune cells are the core mechanism of the development of psoriasis[4]. Genetic, environmental and behavioral factors are thought to be triggers that contribute to the onset of psoriasis[5]. A review of the literature showed that psoriatic arthritis affects between 1.3% and 34.7% of patients diagnosed with psoriasis[6, 7]. Between 4.2% and 69% of all patients suffering from psoriasis develop nail changes[8-10]. Psoriasis causes a great physical, emotional and social burden. Quality of life (QoL), in general, is often significantly impaired[11]. The onset of psoriasis was bimodal with two peaks of the disease, the first between 16 and 22 and the second between 57 and 60 years of age[12]. Numerous studies have reported the coexistence of psoriasis and other serious systemic diseases. Even children show increased rates of comorbidity compared to unaffected infants, or those with atopic eczema[13]. Frequency of metabolic syndrome, depression and erectile dysfunction has also been found to be significantly higher in patients diagnosed with psoriasis[14]. In a study conducted on 200 patients attending tertiary level dermatology clinic, the estimated cost of illness for patients with psoriasis on phototherapy was 22030 rupees per person per year, including costs due to hospitalization and the number of patients on methotrexate was 4213 rupees[15].

Psoriasis is not only a disease that causes painful, debilitating, highly visible physical symptoms. It is also associated with a multitude of psychological impairments. In a study of 127 patients with psoriasis, 9.7% reported a wish to be dead and 5.5% reported active suicidal ideation at the time of a study[16]. Psoriasis can affect relationships at home, school or work as well as sexual relationships and thus reduce QoL and cause psychological strain[11]. In patients with psoriasis, functional impairment, lost opportunities in professional life and elevated economic burden for treatment expenses can add to the significant socioeconomic burden on an individual level[17]. Globally, there is a high need for psoriasis patients for the remission of skin lesions and for relief from the psychosocial burden of disease[18].

The skin diseases are classified as 18 in Siddha system of medicine. These diseases are commonly classified under kuttam. Psoriasis, vitiligo, eczema, Hansen's disease, tinea infections of the skin are also classified under kuttam[19]. The clinical features of psoriasis may be correlated with signs and symptoms of Thadippu Perunoi (Thetthru kuttam) in Siddha. In Siddha, kalanjagapadai is another term compared to psoriasis[20]. It is well known that the Siddha medicines are very good in treating skin diseases especially psoriasis. Some of the well-known medicines in Siddha for treating psoriasis are vetpaalai thailam (oil), arugan thailam (oil), parangipattai chooranam (powder), parangipattai padhangam (Sublimated powder), palagarai parpam (Calx), sangu parpam (Calx), gandhaga chunnam, gandhaga rasayanam. The research in psoriasis doesn't always make headlines or win funding like discoveries in cancer or heart disease. Unlike many other diseases, experiments on mice or other animals aren't very

helpful[21]. So the clinical trial is more appropriate, despite the fact that psoriasis is incurable, it responds well to many topical and systemic treatments. Hence the Siddha trial drugs Panchamuga chendhuram (PMC), Kundavaadhi tailam (KVT) were chosen for this study. The anti-psoriatic activity of ***PMC*** was already estimated in human keratinocyte cell lines (**HaCaT**). The PMC has shown IC_{50} 20 µg/ml, in 24 h with good antiproliferative activity when compared with Asiaticoside as a positive control with an IC_{50} value of 20.13µg/ml.

MATERIALS AND METHODS

Raw drugs were purchased from the Raw drug shop, R. N. Rajan and co., Parry's, Chennai. Authentication was made by Sasikala Ethirajulu, (Consultant) Pharmacognosist, Siddha Central Research institute, Chennai and Purification was made as per the Siddha classical literature[22]. Preparation of trial drugs were made as mentioned in Siddha literature[23,24].

Trial registration and ethical clearance

This clinical study was conducted after getting approval from the IEC (Institutional ethical committee), Government Siddha Medical College (GSMC), Chennai IEC no. **GSMC-CH-ME-2/014/2013**. This trial was also registered in (CTRI) Clinical Trial Registry of India, CTRI no. **CTRI/2014/07/004758.**

Subject selection

Table 1: Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Age 18-60 years.	Pregnancy and lactation
Patches with Scaling.	Leprosy
Redness	Narcotic addicts
Auspitz Sign ±	SLE, Progressive systemic sclerosis
Koebner's Phenomenon ±	Evidences of secondary infection in the lesions
	Cardiac disease
	HIV

Efficacy assessment

In assessing the severity of psoriasis, more than 40 different tools are being used[25]. Commonly used measures for scoring the severity of psoriasis include the Psoriasis Area and Severity Index (PASI). Criteria fixed to assess the clinical improvement was as follows, Marked improvement: PASI ≥ 75%, Moderate improvement: PASI 50% < 75%, Mild improvement: PASI 25 ≥ 50%, Poor improvement: PASI > 25%

PASI involves the assessment of Erythema (E), Infiltration (I), Desquamation (D) and Body surface area involvement (A). The PASI score is calculated by the formula:

$PASI = 0.1(Eh \pm Ih \pm Dh)Ah \pm 0.2(Eu \pm Iu \pm Du)Au \pm 0.3(Et \pm It \pm Dt)At \pm 0.4(El \pm Il \pm Dl)Al$

Safety assessment

Safety of internal drug Panchamuga chendhuram (PMC) was assessed by comparing blood parameters such as liver function test (Total bilirubin, Total protein, SGOT, SGPT, Alkaline phosphatase), Renal function test (urea, creatinine, uric acid) at baseline and after 48 days of treatment.

Study objective

A primary objective is to evaluate the efficacy of Siddha trial drugs "Panchamuga Chendhuram (PMC)" (Internal) and "Kundavaadhi Thailam" (External) on Psoriasis at baseline and after 48 days of treatment. A secondary objective is to evaluate the safety of the trial drug PMC in Psoriasis patients at baseline and after 48 days of treatment.

Study design

Internal Drug: Panchamuga chendhuram (PMC), 65 mg, twice daily.
External Drug: Kundavaadhi thailam (KVT).
Study period: 48 days, **Sample size:** 40 cases
Group I: 20 patients treated with internal drug PMC alone, Group II: 20 patients treated with both internal drug PMC and external drug KVT.

Study Center

Post graduate Department of Sirappu Maruthuvam, Government Siddha Medical College and Hospital, OPD and IPD of Arignar Anna Government Hospital of Indian medicine and Homeopathy, Arumbakkam, Chennai-106. Subjects provided written informed consent; the protocol and consent were approved by institutional review boards or ethics committees. Patients were asked to come for review every week.

Study endpoint

The Primary endpoint is the percentage of improvement in PASI score from baseline and after 48 days of treatment in Group 1 and Group 2 patients. The Secondary endpoint is no significant change in blood parameters such as liver function test and renal function test at baseline and after 48 days of treatment.

Statistical analysis

Basic descriptive statistics include frequency distributions and cross-tabulations were performed. The quantity variables were expressed as Mean ± standard error mean. A probability value of <0.05 was considered to indicate as statistical significance. Paired 't' test was performed for determining the significance. **(-0987Software:** spss17 version)

RESULTS

Table 2: Baseline and demographic characteristics

S.No	Group I	Group II
Patients randomized, n	20	20
Gender		
Male n (%)	14 (70)	11(55)
Female n (%)	6 (30)	9 (45)
PASI ≥ 75% Mean± SEM (n)	17.52 ± 4.29 (9)	20.42± 5.6 (14)
PASI 50% < 75% Mean± SEM (n)	8.73 ± 1.25 (8)	32.37± 13.3 (4)
PASI 25% ≥ 50% Mean± SEM (n)	7.56 ± 3.5 (3)	30.7 ±21.1 (2)
Total	12.515 ± 2.239 (20)	23.84 ± 4.965 (20)

Baseline refers to the start of the study before the first drug administration**.** SEM Standard Error Mean, (n) is a number of patients.

Table 3: PASI after 48 days of treatment

S.No	Group I	Group II
PASI ≥ 75% Mean± SEM (n)	0.489± 0.325* (9)	1.236 ± 0.298* (14)
PASI 50% < 75% Mean± SEM (n)	3.425 ± 0.492* (8)	12.575 ± 5.275 (4)
PASI 25% ≥ 50% Mean± SEM (n)	4.70 ± 2.205 (3)	19.25 ± 12.45 (2)
Total Mean± SEM (n) P value	2.295 ± 0.531* (20) =0.0004	5.305 ± 1.982* (20) =0.0003

P value* > 0.05 is considered to be statistically significant, SEM Standard Error Mean, (n) is number of patients.

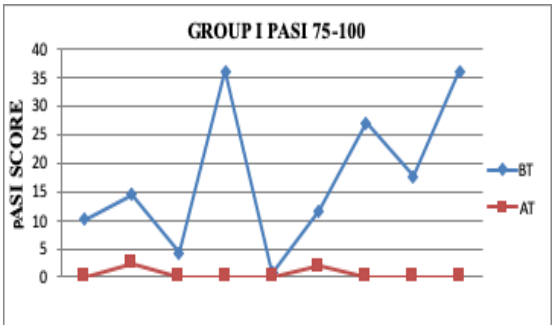


Figure 1: In Group I patients PASI 75-100, 75% or more improvement in Psoriasis Area and Severity Index score from baseline; P value equals 0.0046 this difference is considered to be very statistically significant. BT Before treatment, AT After treatment

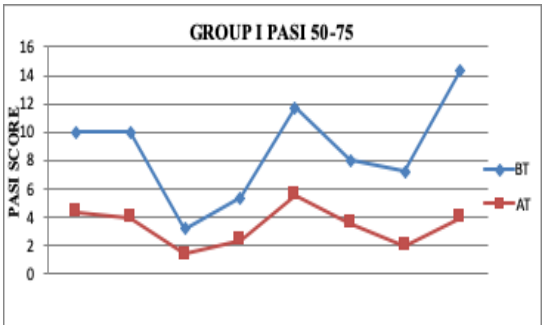


Figure 2: In Group I patients PASI 50-75, 50% to 75% improvement in Psoriasis Area and Severity Index score from baseline; P value equals 0.0006 this difference is considered to be extremely statistically significant. BT Before treatment, AT After

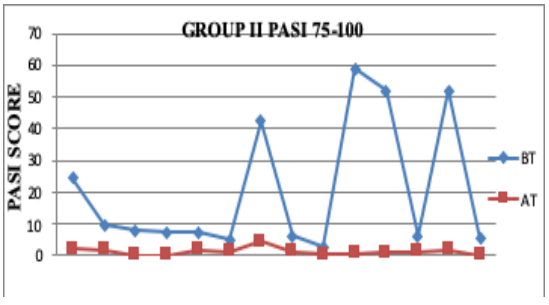


Figure 3: In Group II patients PASI 75-100, 75% or more improvement in Psoriasis Area and Severity Index score from baseline; P value equals 0.0042 this difference is considered to be very statistically significant. BT before treatment, AT after treatment

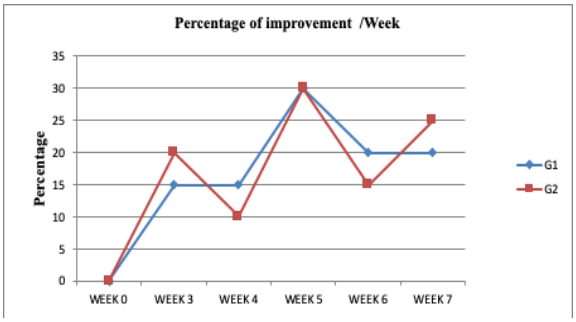


Figure 4: Clinical improvement/ Week. G1 Group I, G2 Group II, Percentage of improvement in PASI score in both the group increases in a timely manner.

Table 4: Liver function test

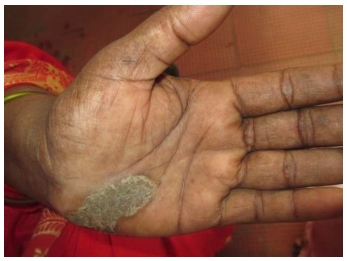
S. No.	Investigations	Before Treatment Mean±SD n= 40	After Treatment Mean±SD n= 40	P value
1	Total Bilirubin	0.80±0.19	0.75±0.17	**<0.05**
2	Total Protein	7.06±0.46	7.02±0.43	**0.361**
2	SGPT	25.73±11.10	25.60±10.07	**0.798**
3	SGOT	25.31±7.72	23.78±7.43	**<0.05**
4	Alkaline Phosphates	82.40±45.87	79.71±26.76	**0.436**

Confidence Interval (C. I): 95%; Paired samples t-test. Where p<0.001, p<0.05 represents statistically significant.

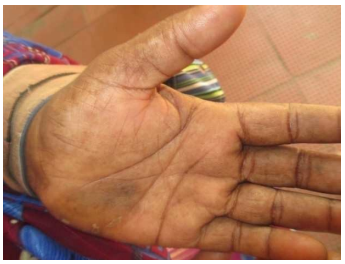
Table 5: Renal function test

S. No.	Investigations	Before Treatment Mean±SD n= 40	After Treatment Mean±SD n= 40	P value
1	Urea	20.57±5.75	20.48±5.48	**0.810**
2	Creatinine	0.67±0.17	0.69±0.21	**0.207**
3	Uric Acid	4.87±1.60	4.88±1.48	**0.836**

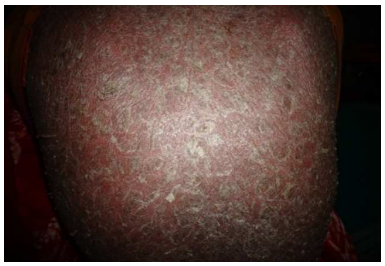
Confidence Interval (C. I): 95%; Paired samples t-test. Where p<0.001, p<0.05 represents the statistical significant.



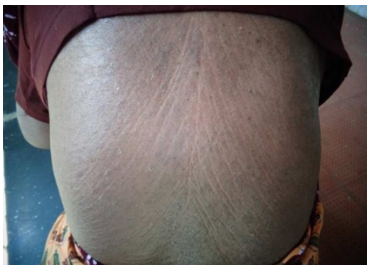
Before treatment (Palmar Psoriasis)



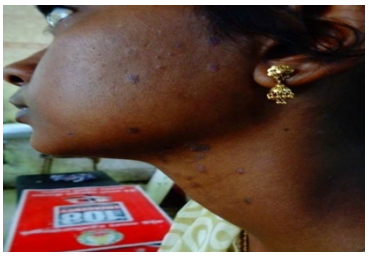
After treatment(Palmar Psoriasis)



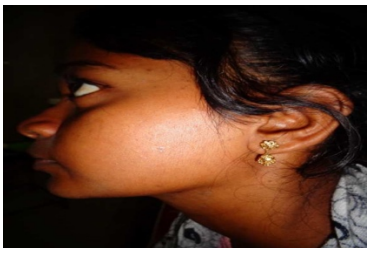
Before treatment (Exfoliative Psoriasis)



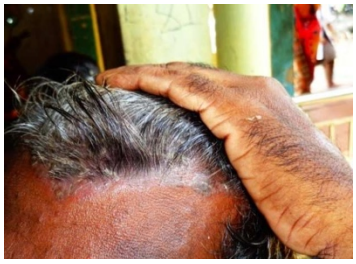
After treatment (Exfoliative Psoriasis)



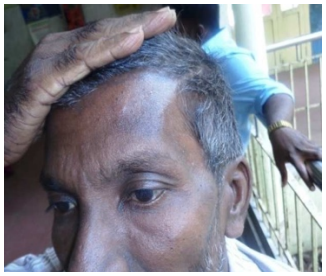
Before treatment (Guttate)



After treatment (Guttate Psoriasis)



Before treatment (Scalp Psoriasis)



After treatment (Scalp Psoriasis)

Figure 5: Improvement of the patients treated with Siddha Drugs Panchamuga Chendhuram (PMC) (Internal) and Kundavaathi Thailam (KVT) (external) for 48 days

DISCUSSION

The Siddha trial drugs PMC, KVT were evaluated for efficacy and safety in psoriasis patients. No serious adverse events, discontinuations due to adverse events, or deaths occurred during this trial. Patients in both groups I and II showed significantly greater improvements in PASI ≥75, PASI 50-75, PASI-25-50 responses through 48 days of treatment. The onset of action of PMC and KVT was rapid, with significant response observed as early as week 3 (Fig 4). Both groups showed no notable differences in safety outcomes through 48 days of treatment.

Efficacy throughout the trial 48 days

In this study, males are commonly affected than female, in group I there was 70% of male and 30% of female patients, whereas in Group II there were 55% of male, 45% of female patients (Table 2). In Group I, 9 patients (45%) achieved more than 75% of the improvement in PASI score, 8 patients (40%) achieved 50%-75% of the improvement in PASI score (Fig 1, 2). In Group II, 14 patients (70%) achieved more than 75% of the improvement in PASI score, 4 patients (20%) achieved 50%-75% of the improvement in PASI score (Fig 3). Complete clearance of psoriasis PASI 100, was observed in 9 patients (22.5%) out of 40 patients. Since the P value is highly significant (<0.001). The drugs PMC and KVT were effective, but the comparison of 2 groups is not statistically significant P value (= 0.1506). Percentage of improvement in PASI score was seen in both the groups from 3rd week onwards. A maximum number of patients in both the groups (6) (30%) had attained significant improvement in 5th week itself. Hence the Siddha trial drugs PMC and KVT were effective in short duration is one of the major advantages, but the nature of the diseases is relapsing we need to do the cohort trial for standardization of the drug. This study was limited by small sample size (40 n) and short duration of treatment (48 days). Studies examining long term efficacy and safety are needed. Hence it is concluded that the treatment was effective and significant. It is also proved that the trial drugs were good in treating all types of psoriasis. Not only plaque psoriasis they were good in psoriatic exfoliation, guttate psoriasis. In patients with scalp psoriasis, palmo-plantar which is often resistant to any treatment was well treated with the trial drugs PMC and KVT.

Safety throughout the trial 48 days

The consequence is often life-long treatment; therefore, all treatments for psoriasis must meet high-quality criteria that are not only efficacious but also safe over long periods. The liver function test and renal function test were taken at baseline and after 48 days of treatment. Though there is a significant change in Bilirubin and SGOT (<0.05) before and after treatment it is minimal and negligible. Whereas the p values of other safety parameters such as T. Protein, SGPT, alkaline phosphatase, urea, uric acid, creatinine are 0.361, 0.798, 0.436, 0.810, 0.207, 0.836 respectively. Hence the liver and renal parameters before and after treatment are not significant ie. No significant change in the values. No gastritis is observed in the patients treated with PMC. KVT was well tolerated there was no skin irritation. Hence the drugs were proved to be safe. The safety data generated from this study helps to conduct future trials in other indications mentioned in classical Siddha text Pulippani vaidhyam -500 for the trial drug PMC.

CONCLUSION

It is vital to create low-cost, effective treatment options that can be made widely available. From the present study, it is clear that the Siddha herbo-mineral formulations are less expensive than the other therapies and therefore, provide a viable alternative for psoriasis management. The drug PMC was effective in the short duration of treatment in a very little amount of dose are other advantages. The trial drugs are affordable, effective and safe in the short term. Further, this research should be carried out in large scale population in the long term to rule out its long term safety.

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