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Research Article

Preclinical and Clinical efficacy of Siddha drug *Karisalankanni Chooranam* in the management of *Pandu Noi* (Iron Deficiency Anaemia)

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ABSTRACT

Siddha system is said to be one among the Indian system of medicines which deals with Five Boodhas and Three Humours in the diagnosing and treatment aspect of a disease. Siddhars classified diseases as 4448 types. *Paandu Noi* is one among them. *Paandu Noi* symptoms are more or less equivalent to Iron deficiency anaemia. Iron Deficiency Anaemia (IDA) is a very common disease prevalent in the society. Long term oral iron therapy is commonly used as first line therapy but iron salts such as ferrous sulphate are associated with a high incidence of gastrointestinal side effects such as nausea, vomiting, diarrhoea or constipation. Because of their adverse effects, a safe, effective, cheap, and easily available drug is needed. Many drugs are available in Siddha system of medicine which have remarkable effects in treating anaemia. One such medicine is Karisalankanni chooranam is indicated for anaemia mentioned in Siddha classical literature.

With the aim of that, this Poly Herbal preparation may be effective to manage childhood IDA without any synergistic effects. The present study was carried out to study the efficacy and safety of the Siddha poly herbal compound drug karisalankanni chooranam with the application of modern parameters. The Karisalankanni chooranam reveal no toxicity in the preclinical studies and hence proven to be safe for human administration.

From the pre- clinical pharmacological study it is evident that the trial medicine has significant Haematinic action. Also Karisalankanni chooranam has been proved clinically. Since as it raises the haemoglobin level in a marked level to the patients given regularly for not less than 30 days along with supplementary diets. Both symptomatic and qualitative improvements were absorbed. For prognosis, routine haematological investigation was taken. During the treatment no adverse events were observed. Statistically it has been proved that it shows significant raise in the haemoglobin level.

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BACKGROUND

Siddha system is said to be one among the Indian system of medicines, i.e., it is one in the AYUSH group. Siddhars are those who lived and maintained their body as they desired best. There are various principles present in Siddha system said by different Siddhars. The major and common concept of Siddha deals with Five Boodhas and Three Humours, respectively *Prithivi, Appu, Theyu, Vaayu, Aagayam* along with Vatham, *Pitham and Kapham.*

The physiology, pathology, diagnosis and treatment in siddha is based on the above said three humours. When these Humours in the human body get affected, it is said to be *Dhosha or kutram.* The fluctuations of these humours leads to disease, the repair of these kutrams is the treatment procedure in Siddha.

Our Siddhars, not only concentrated on the diagnosis and treatment, they have followed and given a various principles to lead a healthy and hygienic life. Siddha is built by vast number of Siddhars, such as *Navanadhasiddhar, padhinensiddhar, navakodisiddhar, navasiddhar*. In this, *padhinen siddhargal* plays a major role in the Siddha system.

Agathiyar is said to be the first siddhar in padhinensidhargal. He have described that there are 4448 diseases in his book *Agathiyar rathna churukka naadi*. It includes 62 types of diseases and its classifications. According to this, Paandunoi is classified into 10 types.

Paandunoi symptoms are more or less equivalent to Iron deficiency anaemia. Iron Deficiency Anaemia (IDA) is a very common disease prevalent in the society. Long term oral iron therapy is commonly used as first line therapy but iron salts such as ferrous sulphate are associated with a high incidence of gastrointestinal side effects such as nausea, vomiting, diarrhoea or constipation. Because of their adverse effects, a safe, effective, cheap, and easily available drug is needed. Many drugs are available in Siddha system of medicine which have remarkable effects in treating anaemia. One such medicine is ***Karisalankanni chooranam***, which is indicated for anaemia in Siddha classical literature.

With the aim of that, this Poly Herbal preparation may be effective to manage childhood IDA without any synergistic effects. The present study was carried out to study the efficacy and safety of the Siddha poly herbal compound drug ***karisalankanni chooranam*** with the application of modern parameters.

OBJECTIVE:

To evaluate the efficacy of Herbal Formulation ***karisalankanni chooranam*** in the treatment of ***iron deficiency anaemia*** (IDA).

MATERIALS AND METHODS

STUDY DESIGN

An open clinical trial on paandu noi was carried out in the OP of P.G Kuzhanthai Maruthuvam Department attached to Aringnar Anna Hospital of Indian Medicine, Chennai-106.

The study was approved by Institutional Ethical Committee (IEC) and approval number is **GSMC-CH-ME-2/01/20182017**

POPULATION AND SAMPLE:

The population consists of all patients satisfying the inclusion and exclusion criteria mentioned below. Sample consists of paandunoi patients who were attending the OP of Aringnar Anna Hospital, Arumbakkam, Chennai- 106.

SAMPLE SIZE:

The study is considered in 40 selected patients of both genders between age groups of 3-12 years.

INCLUSION CRITERIA:

- Age: 3-12 years
- Hb level between 7-12 gms
- Worm infestation
- Angular stomatitis
- Pallor of the skin, mucous membrane, nail bed and conjunctiva.
- Lack of concentration and poor school performance
- Fatigue
- Constipation

EXCLUSION CRITERIA:

- Known H/O of Metabolic disorder
- Known H/O of Haemolytic anaemia
- Patient with previous blood transfusion
- Patient with any other serious illness.

WITHDRAWAL CRITERIA:

- Exacerbation of symptoms.
- The subject develops adverse drug reactions and adverse event they will be withdrawn from the trial.
- Patient turned unwilling to continue in the course of clinical trial.

EVALUATION OF CLINICAL PARAMETERS:

Patients are clinically evaluated by using the following parameters

a. History taking:

Age, occupation, Socio economic status, complaints and duration, past illness, family history, and personal habits were recorded in the case sheets for every patients during his / her first visit to OP.

b. INVESTIGATIONS:

Blood : TC, DC, ESR, Hb

Urine : Albumin, Sugar, Deposit

c. SPECIFIC IVESTIGATIONS:

Blood : PCV, MCV, MCH, MCHC, Total RBC

Motion: Ova, Cyst, Occult blood

d. CLINICAL DIAGNOSIS BASED ON SIDDHA SYSTEM:

The parameters used to diagnose the disease *paandu Noi* in siddha system are as follows,

- ***Poriyalaridhal-*** Examination of five sensory organs – (AIYMPORI): Skin, Tongue and buccal cavity, Eyes, Nose and Ear (MEI, VAI, KANN, MOOKU and SEVI)
- ***Pulanaalaridhal-*** Examination by physical perception – (IYMPULAN): Taste, Vision, Tactile sensation, Sound and Smell.
- ***Vinaadhal-*** Examination by interrogation, which includes history of illness, examination by the physician by using his organs of sensory perception.
- ***Uyirthathukkal–***Examination of Physical constituents of body
- ***Udalthadhukkal-*** Examination of body tissues
- ***Envagaithervu -*** Eight basic diagnostic parameters namely Naadi (pulse), Sparism (Touch), Naa (Tongue), Niram (colour), Mozhi (speech), Vizhi (Vision), Malam (Motion) and Moothiram (Urine)

STATISTICAL ANALYSIS:

Data analysis will be done in Microsoft excel 2013 and SPSS software.

QUALITY ASSURANCE:

The quality of the study will be assured as the whole study will be conducted in supervision of faculties of the department and guide of the study.

ETHICAL CONSIDERATIONS:

No ethics were violated during the study as the participants were included only after explaining the need of study and study procedure. Study was conducted only after getting official consent/Assent obtained. Confidentiality was maintained throughout the study.

STUDY INTERVENTION:

Figure 1: Karisalankanni chooranam

DOSE: 200mg – 500mg twice a day dispensed in dry and clean pet bottles.

ADJUVANT: Honey

DURATION: 28 days

INGREDIENTS&QUANTITY: (1 thola = 10 gms)

NAME	BOTANICAL NAME	PARTS USED	QUANTITY
Karisalankanni	*Eclipta prostrate*	Dried whole plant	4 thola
Mookirattai	*Boerhaevia diffusa*	Dried whole plant	1 thola
Chukku	*Zingiber officinale*	Dried rhizome	1 thola
Milagu	*Piper nigrum*	Dried seed	1 thola
Thippili	*Piper longum*	Dried fruit	1 thola
Kadukkaai	*Terminalia chebula*	Dried fruit coat	1 thola
Nellikkaai	*Phyllanthus emblica*	Dried fruit	1 thola
Thandrikkaai	*Terminalia bellerica*	Dried fruit coat	1 thola
Maramanjal	*Coscinium fenestratum*	Dried wood	1 thola
Thaniya	*Coriandrum sativum*	Dried fruit	1 thola
Athimathuram	*Glycyrrhiza glabra*	Dried root	1 thola
Karunseeragam	*Nigella sativa*	Dried seed	1 thola
Thalisapathiri	*Abies spectabilis*	Dried leaves	1 thola
Elam	*Elettaria cardamomum*	Dried seed	1 thola
Seeragam	*Cuminum cyminum*	Dried seed	1 thola

Table 1: Drugs of karislankanni chooranam along with its quantity

The medicine was prepared after getting authentication from the Head of the department of Department of Bio-chemistry and the medicine was prepared under the guidance of staffs of Department of Gunapadam at the laboratory of Gunapadam, Government Siddha Medical College and Hospital, Palayamkottai.

PRE CLINICAL SCREENINGS

Biochemical Analysis:

Qualitative Analysis of the trial drug revealed the presence of iron, chloride, calcium, starch, reducing sugar.

Phytochemical Analysis:

The phytochemical analysis of the trial drug shows that the drug contains Glycosides, Carbohydrates, Coumarins, Phenols.

Physico chemical Analysis:

Loss on drying at 105^0C - 2.43%
Total ash - 17.6%
PH - 5
Acid insoluble ash - 0.26%
Water soluble extractive - 26%
Alcohol soluble extractive - 12%

TOXICITY STUDY OF THE DRUG:

Acute toxicity:

Acute and sub acute toxicity studies were conducted on experimental rats at C. L. Baid Metha College of Pharmacy, Chennai, Tamilnadu (IAEC NO: LV/11/CLBMCP/2018). Acute toxicity study of the drug k was carried out as the OECD guideline-423 (Organisation to Economic Co-operation and Development). The acute toxicity study of my trial drug was studied and the drug was proved safer for long term administration, as it did not exhibit any significant toxicity at 2000 mg / kg body weight.

Sub acute toxicity:

Sub acute toxicity study as per the guideline of – 407. Under the dosage of trial drug 200mg / kg (Low dose), 400mg / kg (High dose) it did not exhibit any significant.

Histo pathology:

At the end of toxicity studies the animal were sacrified and they were subjected to hematological parameters (TC, DC & Hb) chemical parameters (LFT, RFT) and histopathology of vital organs like Liver, Kidney, Spleen, Lungs were carried out. The studied did not exhibit the evidence of remarkable pathological lesions in the tissues.

Pharmacological activity

The pharmacological studies of trial medicine *Karisalankanni chooranam* showed significant Haematinic action wistar albino rats.

Haematinic action of *Karisalankanni chooranam* was carried out by producing anemia by administrating a single intramuscular injection of desferrioxamine at a dose of 15mg/kg b.w. Drop out period of four days was awaited until the sufficient drop in Hb level was noticed in animals. Rats were considered as anaemic model if haemoglobin concentration was less than 14g/dl. Then the trial drug was administered show a potent haematinic action during the studies.

RESULTS

S.NO	AGE	BEFORE Gms/dl	AFTER Gms/dl	DIFFERENCE
1	11/Fc	11.5	12	**0.5**
2	10/Fc	10.3	12.2	**1.9**
3	08/Mc	11.5	11.8	**0.3**
4	06/Mc	11.1	11.5	**0.4**
5	09/Mc	9.2	10.5	**1.3**
6	08/Fc	12	11.5	**-0.5**
7	08/Fc	12.9	12.5	**-0.4**
8	12/Fc	11.7	11.9	**0.2**
9	09/Fc	10.4	11.2	**0.8**
10	10/Fc	11.6	12	**0.4**
11	12/Fc	9.9	11	**1.1**
12	08/Fc	7.1	10.2	**3.1**
13	$6^{1/2}$ /Fc	12.1	12.5	**0.4**
14	08/Fc	13.1	12.8	**-0.3**
15	07/Fc	12.4	12.1	**-0.3**
16	09/Mc	12.9	12.8	**-0.1**
17	08/Mc	8.6	10.2	**1.6**
18	06/Fc	8.8	10.8	**2**
19	06/Mc	13.4	13.4	**0**
20	09/Fc	11.9	12	**0.1**
21	06/Fc	12.1	12	**-0.1**
22	07/Fc	8	10.2	**2.2**
23	11/Mc	13.1	13.2	**0.1**
24	06/Mc	12.2	12.4	**0.2**
25	08/Mc	12.3	12.5	**0.2**
26	08/Mc	12.2	12.8	**0.6**
27	10/Fc	14.3	14	**-0.3**

28	07/Fc	12.4	12.6	**0.2**
29	$6^{1/2}$/Mc	13.4	13	**-0.4**
30	12/Fc	12.7	12.6	**-0.1**
31	06/Mc	11.3	11.2	**-0.1**
32	12/Mc	11.8	11.5	**-0.3**
33	08/Fc	11.6	11.2	**-0.4**
34	$8^{1/2}$/Mc	13	15	**2**
35	06/Mc	11.2	12	**0.8**
36	10/Mc	12	12.4	**0.4**
37	07/Fc	9	10.2	**1.2**
38	11/Fc	11.2	12	**0.8**
39	08/Fc	11.8	12.2	**0.4**
40	08/Fc	12	12.5	**0.5**
	MEAN	**11.5**	**12.01**	**0.51**
	St.dev	**1.58**	**1.035**	**0.84**

Table 2: Hb count of Patients before and after treatment

Mean value of HB before treatment: 11.5 ± 1.57
Mean value of Hb after treatment 12.01 ± 1.03

To analyse the significance, Paired T- Test is chosen

T- Test of Paired sample		
	Variable 1	***Variable 2***
Mean	**11.5**	**12.01**
Variance	**2.495897436**	**1.072205128**
Observations	**40**	**40**
Pooled Variance	**1.784051282**	
Hypothesized Mean Difference	**0**	
Df	**78**	
t Stat	**-1.707581759**	
P(T<=t) one-tail	**0.045845808**	
t Critical one-tail	**1.664624645**	

Table 3: Statistical analysis before and after treatment

- -Null Hypothesis: There is no difference between means
- -Alternate Hypothesis: There is absolute difference between two means **P- Value= 0.04**
- -If the P-Value is less than 0.05, then the null hypothesis is rejected
- -As the P-Value of this study is 0.04, Null Hypothesis is rejected and Alternate hypothesis is accepted. Thus concluding that there is difference in the means of before and after treatment.
- -To signify the difference, Pearson correlation between two variables taken which shows the result of **0.87 (87%)**

Table 4: Strength of Correlation

Coefficient of Correlation	
Value of r	**Strength of relationship**
-1.0 to -0.5 or 1.0 to 0.5	**Strong**
-0.5 to -0.3 or 0.3 to 0.5	**Moderate**
-0.3 to -0.1 or 0.1 to 0.3	**Weak**
-0.1 to 0.1	**None or very weak**

- As the r value of this study is 0.87, it shows that the result has Strong Positive correlation
- i.e statistical correlation is measured by what is called the co-efficient of correlation(r). Its numerical value ranges from +1.0 to -1.0.
- It gives us indication of both the strength and direction of the relationship between variables.

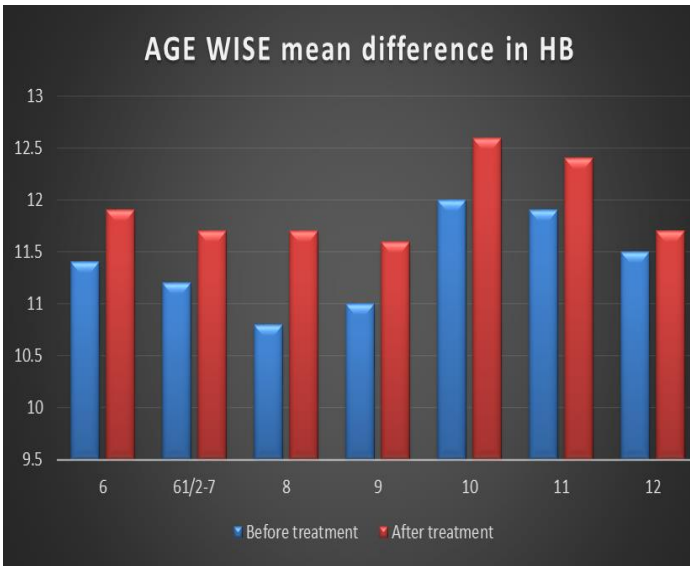

Figure 2: Age wise mean difference before and after treatment

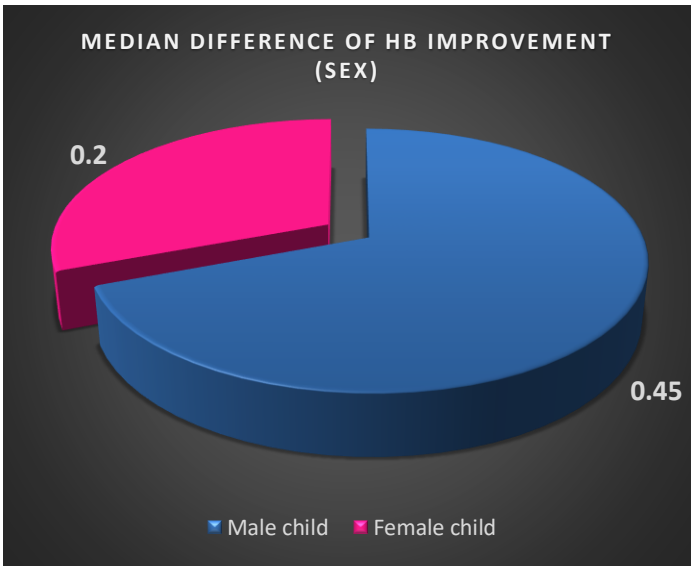

Figure 3: Sex wise mean difference before and after treatment

SUMMARY

To study the efficacy of Siddha trail drug ***Karisalankanni chooranam*** as internal medicine for the treatment of Paandu Noi in children. This disease mostly resembles Iron deficiency anaemia in modern system. Literature evidences of both Siddha and Modern system were collected and also the ingredients of the trial drug were reviewed as well. For the clinical study, 40 patients were selected based on protocol. This study is conducted after the drug being screened by the Screening committee and approved by the Institutional Ethical Committee (IEC) of Govt. Siddha medical college Chennai.

Selected patients with Paandu Noi diagnosed clinically treated in outpatient department of Govt. Siddha medical college attached with Arignar Anna Hospital of Indian Medicine, Chennai-106. They were undergone laboratory investigation and treated with trial drug, observed for clinical improvement and any adverse reaction. Qualitative analysis of the ***Karisalankanni chooranam*** presence of iron, calcium, starch, chloride and Reducing sugar. Phytochemical analysis of the trial drug shows that presence of Glycosides, carbohydrates, coumarins, phenol. Physico chemical analysis of the trail drug shows the pH 5, Total ash value 17.6% shows the safe and effectiveness of the trial drug.

Toxicological studies shows that, it has no significant toxic effect. From the preclinical pharmacological study shows that the drug has got a significant haematinic activity. Among the 40 patient's good improvement was observed in 20 cases (50%),

moderate improvement in 13 cases (32.5%) and mild improvement in 7 cases (17.5%).

CONCLUSION

Paandu noi is mainly caused by the derangement of Pitham followed by vatham and kabam. The deranged kuttram is settled down by the kaippusuvai in the trial drug there by medicine act effective in cure the disease. In physico chemical Analysis iron was found to be present as effective ingredients in treating anaemia.

The Karisalankanni chooranam reveal no toxicity in the preclinical studies and hence proven to be safe for human administration. From the pre- clinical pharmacological study it is evident that the trial medicine has significant Haematinic action. Also Karisalankanni chooranam has been proved clinically. Since as it raises the haemoglobin level in a marked level to the patients given regularly for not less than 30 days along with supplementary diets. Both symptomatic and qualitative improvement was absorbed. For prognosis, routine haematological investigation was taken. During the treatment no adverse events were observed. Statistically it has been proved that it shows significant raise in the haemoglobin level. Hence it is concluded that the trial drug Karisalankanni chooranam will be a better drug that can be used in the treatment of Paandu Noi.

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