

Abstract

Background: *Panduroga* is one of the major categories of diseases described in Ayurveda with its own specific etiopathogenesis and treatment. It is such a disease where *pandutva* (discoloration of skin) has been given much importance and so it has been named as *Panduroga*. It is a disease that closely resembles the clinical picture of Anaemia. Anaemia is the world's most common nutritional deficiency disorder. In this disease Pallor of the skin is caused due to decrease in haemoglobin, the number of RBCs per cumm of blood, the amount of Hb percent and a lack of iron. Anemia is the leading cause of nutritional anaemia in more than half of preschool and adolescent children. As per WHO, this disease affects globally 1.62 billion people which corresponds to 24.8% of population. Highest prevalence is found in preschool age children i.e 47.4% **Aim:** The present study is aimed to Compare the efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in *Pandu* with special reference to Iron Deficiency Anemia. **Material & Methods:** The present study is designed as open label Randomized Standard Reference Control Clinical Trial, in which minimum 120 patients will be enrolled in two groups. In Group A (Standard control) –*Dadimadi Ghrita* will administered as per age of patient and in Group B (Trial) –*Rajanyadi Ghrita* will be administered twice a day with warm water after meal for 30 days. Assessement will be recorded on 15th, 30th and 60th day. **Results:** Changes will be observed in subjective parameters such *Agnimandya*, *Shrama*, *Bhrama*, *Aruchi*, *Kopana*, *Nidralutwa* and objective parameters such as CBC with Peripheral smear. **Conclusion:** Suitable conclusion will be drawn post completion of the trial.

Keyword- Anemia, *Dadimadi Ghrita*, *Pandu*, *Rajanyadi Ghrita*

INTRODUCTION-

Panduroga is one of the major categories of diseases described in Ayurveda with its own specific etiopathogenesis and treatment. It is such a disease where *Pandutva* (discoloration of skin) has been given much importance and so it has been named as *Panduroga*¹, due to prominence of pallor of skin. It develops due to depletion of *Rasadhatu* with the association of other *Dhatu* and *Tridosha* which in turn becomes ineffective the production of *Raktadhatu*². *Pitta dosha* plays the major role in the pathogenesis of *Panduroga* and thus body metabolism is grossly affected in this condition which is evident in the general clinical features such *Karnasweda* (as ringing sound in ears), *Aruchi* (loss of appetite), *Daurbalya* (general debility), *Annadwesa* (aversion towards food), *Shrama* (tiredness), *Bhrama* (giddiness), *Gatramarda* (body ache), *Panduta* (loss of complexion) and *Shwas* (breathlessness). the main feature of *Panduroga* is *Pandutva*. According to Charaka, it is one among the *Rasavaha Srotodushti*³. Susrutacharya explained it in *Raktavaha Srotodushti*.

It is a disease which shows great similarity to the clinical picture of Anaemia. It is the most common nutritional deficiency disorder in the world. In this disease reduction of haemoglobin and number of RBCs per cumm of blood resulting in pallor of skin⁴. Nutritional deficiency anemia is very common in India and iron deficiency is the commonest nutritional deficiency all over the world. Children, adult male, Females suffer the most form of this. Anemia resulting from lack of sufficient iron for synthesis of hemoglobin is the common hematologic disease of infancy & childhood.

Iron Deficiency Anemia is the most common cause of nutritional anemia in > 50% of preschool & adolescent children. According to WHO, anemia affects globally 1.62 billion people which corresponds to 24.8% of population. Highest prevalence is found in preschool age children i.e 47.4%⁵ Iron is a mineral found in the bloodstream that is necessary for growth, enzyme development and function, immune system health, energy levels, and muscle strength. It is an essential component of haemoglobin and myoglobin, a type of haemoglobin found in muscle tissue. PCV levels also fall in iron deficiency Anaemia.

Nutritional anemia are the condition in which individual's haemoglobin concentration is below the normal level due to a deficiency of one or more nutrients required for hemopoiesis, and the haemoglobin can be increased by nutrient supplementation. Iron, folate, vitamin B12, proteins, and vitamin E are the most important nutrients. Iron is also required in greater quantities during

the first few years of life, adolescence, menstruation, pregnancy, and lactation⁶. Iron Deficiency Anemia is caused by insufficient dietary intake and improper iron absorption. Symptomatology depends on rate of fall in hemoglobin & hemostatic adjustment of various disease which presents with the significant symptoms such as feeling of weakness, tiredness, shortness of breath, palpitations, Koilonychia, Glossitis, Dysphagia and altered sensation of taste⁷.

Dadimadi Ghrita and *Rajanyadi Ghrita* is explained in the context of *Pandu Roga* in *Ashtang Hridaya*. Both the formulations are having *pandu roga hara* property.

Need of the study

According to WHO and National Family Health Survey, Anaemia affects 70-80 percent of children. It is common in India due to a low dietary intake, a lack of iron availability, chronic blood loss, and malabsorption⁸. Various iron salts, the most common of which is ferrous sulphate, have been used to treat IDA. Oral iron use is primarily limited by its GI side effects (Nausea, Flatulence, Abdominal pain, Diarrhoea, Constipation, Black & Tarry stools⁹), intolerance to oral iron, and the need for rapid recovery due to the long duration of therapy. Minimal research studies had been carried out with *Dadimadi Ghrita* specifically in Iron Deficiency Anemia of children but no comparative studies have been conducted as the protocol of present study. No research studies are conducted on the efficacy of *Rajanyadi Ghrita* in *pandu* till date. With the aim that herbo mineral medicines may be effective to manage childhood IDA without any side effects, the present study was carried out to study the efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in *Pandu* with special reference to IDA. *Rajanyadi ghrita*¹⁰ is explained in the context of *Pandu Roga* in *Ashtang Hridaya Uttarsthan*. It has properties of *Agnidipan* and *Vatanulomana*, *Paduhara*, *Baal* and *Varna* enhancer. It is a medicated *Ghrita* processed with *Rajani*, *Daru*, *saral*, *Shreyasi*, *Bruhati*, *Kantkari*, *Prushni parni*, *Shatavh* and *makshika*. While, *Dadimadi Ghrita*¹¹ is explained in the context of *Pandu Roga* in *Ashtang Hridaya Chikitsasthan*. It has properties of *Deepan*, *Vatanulomana*, *Shwas Kasaghana*, *Panduhara*, *Pliharoga*. It is a medicated *Ghrita* processed with *Dadimba*, *Dhayaka*, *Pipalli*, *Sunthi*, *Chitraka* and *Ghrita*.

Research Question: Whether *Rajanyadi Ghrita* is effective as compared to *Dadimadi Ghrita* in the management of *Pandu* with special reference to Iron deficiency Anemia

Hypothesis-

1. *Rajanyadi Ghrita* may or may not be effective in the management of *pandu* as compared to *Dadimadi Ghrita*.
2. *Rajanyadi Ghrita* as effective as *Dadimadi Ghrita* in the management of *pandu*

REVIEW OF LITERATURE:

Table No.1 – Shows Data Collected from Samhita

Previous works done:

1. Das A, Saritha S. PA03. 17. A clinical evaluation of *Punarnavadi Mandura* and *Dadimadi Ghrita* in management of *Pandu* (Iron deficiency anaemia) *Anc Sci Life*. 2013;32(Suppl 2):S86.
2. Kumar A, Garai AK. A clinical study on *Pandu Roga*, iron deficiency anemia, with *Trikatrayadi Lauha* suspension in children. *J Ayurveda Integr Med*. 2012;3(4):215-222. doi:10.4103/0975-9476.104446
3. Samal J. Ayurvedic preparations for the management of Iron Deficiency Anemia: A systematic review. *Ayu* 2016;37:163-9.
4. Arankalle PS. Effect of *Dadimadi Ghrita* in *Garbhini Pandu* (Anaemia in Pregnancy). *J Ayurveda Holistic Med* 2014;2:1-10

List of previous Thesis:

1. Das A, Saritha S. PA03. 17. A clinical evaluation of *Punarnavadi Mandura* and *Dadimadi Ghrita* in management of *pandu* (Iron deficiency anaemia) *Anc Sci Life*. 2013;32(Suppl 2):S86.
2. Kumar A, Garai AK. A clinical study on *Pandu Roga*, iron deficiency anemia, with *Trikatrayadi Lauha* suspension in children. *J Ayurveda Integr Med*. 2012;3(4):215-222. doi:10.4103/0975-9476.104446

List of published articles with brief conclusions:

1. Das A, Saritha S. PA03. 17. A clinical evaluation of *Punarnavadi Mandura* and *Dadimadi Ghrita* in management of *pandu* (Iron deficiency anaemia) *Anc Sci Life*. 2013;32(Suppl 2):S86.

Outcome- Symptoms were statistically analyzed before and after treatment, there was statistically significant changes ($P < 0.001$) were observed in the signs and symptoms of *Pandu*

rogi(IDA). There was a statistically significant response in hemoglobin and other hematological investigation like MCHC, MCV, PCV, Reticulocyte Count, peripheral Blood smear, serum iron, serum Ferritin and Total Iron Binding Capacity in the Group ($P < 0.001$).

2. Kumar A, Garai AK. A clinical study on Pandu Roga, iron deficiency anemia, with Trikatrayadi Lauha suspension in children. *J Ayurveda Integr Med.* 2012;3(4):215-222. doi:10.4103/0975-9476.104446

Outcome- The present study shows that the trial drug Trikatrayadi Lauha suspension is effective to improve clinical features and hematological parameters significantly. The medicine is effective to increase the hemoglobin level 1.94 g/dL (8.52 -10.46 g/dL, $P < 0.001$) in 5 weeks and 3.33g/dL (8.52 -11.85g/dL, $P < 0.001$) in 10 weeks. No adverse effect of the trial drug was observed during the study.

3. Samal J. Ayurvedic preparations for the management of Iron Deficiency Anemia: A systematic review. *Ayu* 2016;37:163-9.

Outcome- Four studies were focused on the general population. The Ayurvedic formulations studied in these four studies for their efficacy against IDA among general population include Navayasa Lauha, Punarnavadi Mandura, Dhatri Lauha, Pradarantaka Lauha, Sarva-Jvara-Hara Lauha, Brihat Yakrdari Lauha, **Dadimadi Ghrita** and Trikatrayadi Lauha. There are several explanations regarding the efficacy of Ayurvedic formulations in combating IDA in general population. All these studies showed statistically significant results in both subjective and hematological parameters. Another advantage of these Ayurvedic formulations is that they are safe and effective against IDA at all ages and groups.

4. Arankalle PS. Effect of *Dadimadi Ghrita* in Garbhini Pandu (Anaemia in Pregnancy). *J Ayurveda Holistic Med* 2014;2:1-10

Outcome- Relief of anemia was observed among 16 participants up to 51%-75% followed by 8 participants up to 76%-100% and 11 participants up to 26%-50%. Increase of Hb g% was observed among 15 (42.86%) participants up to 1 g%, in 10 (28.57%) participants up to 1.5 g%, in 5 (14.28%) participants up to 0.5 g% and >2 g% in 3 (8.57%) participants.

Research Gaps Analysis- *Rajanaydi churna* with *ghrita* is narrated by Acharya Vaghbhat in Ashtang Hriday Samhita in treatment of *Pandu*. It is one of the popular formulation used to increase immunity in children, treating anemia and GIT related diseases and as tonic powder. But no studies have found on *Rajanaydi Ghrita* in *Pandu*. So to explore the efficacy of this medicated *Ghrita* in *Panduroga* the present study is selected.

AIM AND OBJECTIVES

Aim: Comparing the efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in management of *Pandu* with special reference to Iron deficiency Anemia.

Objectives:

1. To study the etiopathogenesis of *Pandu* in patients and comparing it with etiology given in literatures.
2. To evaluate efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in *Panduroga*
3. To evaluate efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in *Panduroga* in increasing Hb%.

MATERIAL AND METHODS

The study is plan as a Randomized clinical trial to Comparing the efficacy of *Dadimadi Ghrita* and *Rajanyadi Ghrita* in Patients of *Pandu* with special reference to Iron deficiency Anemia in children aged 3 – 15yrs with pre- test and post- test design.

Source of Data: Patients of *Pandu* will be selected from OPD and IPD of Department of Kaumarbhritya, Mahatma Gandhi Ayurved College as well from nearby school of Wardha and special camps.

Study design: Randomized Standard Reference Control Clinical Trial

Drug collection/ authentication: The raw materials required for *Rajanyadi Ghrita* will be procured from local shop and will be verified by Department of Dravyaguna

Detail of Drug Preparation: *Rajanyadi Ghrita* will be prepared as per classical method in Dattatraya Rasashala as per standard protocol and will be analyzed in Pharmaceutical Laboratory and the drug *Dadimadi Ghrita* will purchased from pharmacy attached to hospital.

Sampling procedure: Simple Randomized Sampling by Computer Generated Randomization Chart

The sample size formulae used are as follows:

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2 / \kappa)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_2 = \frac{(\kappa * \sigma_1^2 + \sigma_2^2)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

The notation for the formulae are:

n_1 = sample size of Group 1

n_2 = sample size of Group 2

σ_1 = standard deviation of Group 1

σ_2 = standard deviation of Group 2

Δ = difference in group means

κ = ratio = n_2/n_1

$Z_{1-\alpha/2}$ = two-sided Z value (eg. Z=1.96 for 95% confidence interval).

$Z_{1-\beta}$ = power

Sample size (Including sample size calculation):

Pilot Study Results of MD thesis: 2019 (Randomized Clinical trial on the efficacy of Pathyadi Gutika in Pandu w.s.r. to Iron Deficiency Anemia; Department of Kaumarbhritya MGAC)

Mean pallor score in Group A at day 28 =0.40

Mean pallor score in Group B at day 28 = 0.66

σ_1 =SD of pallor score in Group A at day 28 = 0.50

σ_2 =SD of pallor score in Group B at day 28 = 0.48

For detecting mean difference of 0.26% i.e $\Delta=0.66 - 0.40 = 0.26$

$N1=(0.50*0.50 + 0.48*0.48)(1.96+0.84)^2/(0.26*0.26)$

=55.71 = 60 patients required in each groups

Table No 2 – Shows Grouping & Posology:

POSOLOGY- The drug, *Dadimadi Ghrita* and *Rajanyadi Ghrita* will administered in the following dosage¹² for a period of 30 days.

Table No 3- Shows Posology

Data collection tools and process:

Inclusion criteria-

- Subjects aged 3 to 15 years with *Samanya lakshana* of *Pandu roga* and Iron deficiency Anemia, irrespective of sex, caste & socio economic status
- Subjects with Hb% ranging from 7gm to 11gm.
- Patient/Parents given written consent.

Exclusion criteria –

- Patients with known case of sickle cell anemia, leukemia, Thalessemia and Endocranial disorder etc
- Patients suffering with any infectious diseases
- Patient on medication for Anemia

Diagnostic criteria-

Table no 4. Criteria for diagnosis of *Pandu roga* (Iron deficiency Anemia)

Assessment Criteria:

Subjective parameter:

1. General signs and symptoms of *Pandu* such as *Agnimandya*, *Shrama*, *Bhrama*, *Aruchi* , *Kopana* , *Nidralutwa* .
2. Lakshana of *Pandu* other than above mentioned features

3. Signs and symptoms of Iron Deficiency Anemia

Objective parameter:

1. Hemoglobin percentage
2. Peripheral smear
3. Mean Corpuscular Volume
4. Mean Corpuscular hemoglobin
5. Mean Corpuscular Hemoglobin Concentration

Gradation of Symptoms:

Gradation:

1. Shrama

| | |
|---|---|
| No fatigue | 1 |
| Fatigue occasionally | 2 |
| Fatigue in carrying routine work/playing | 3 |
| Fatigue present even without doing work/playing | 4 |

2. Aruchi

| | |
|---|---|
| Normal instincts of taking food | 1 |
| Feeling to take food not having taste | 2 |
| Not feeling to take food even if hungry | 3 |
| Not interested to taking food | 4 |

3. Brahma (giddiness)

| | |
|--------------|---|
| No giddiness | 1 |
|--------------|---|

| | |
|------------------------|---|
| Occasionally giddiness | 2 |
| Always | 3 |

4. Agnimandya

| | |
|----------|---|
| Absent | 1 |
| Mild | 2 |
| Moderate | 3 |
| Severe | 4 |

5. Kopana

| | |
|------------|---|
| Absent | 1 |
| Occasional | 2 |
| Frequent | 3 |
| Always | 4 |

6. Nidralutwa

| | |
|------------|---|
| Absent | 1 |
| Occasional | 2 |
| Always | 3 |

7. Pallor

| | |
|----------|---|
| Absent | 1 |
| Mild | 2 |
| Moderate | 3 |

Mild ranging- 10 to 11gm/dl

Moderate ranging 7 to 10gm/dl

ANALYSIS PLAN:

Table No 5- Composition of the Formulation : *Dadimadi Ghrita*

Table No 6- Composition of the Formulation: *Rajanyadi Ghrita*

B] Data Analysis (statistical methods): The data will be analyzed by using student T tests, Paired T test Wilcoxon on signed- rank test.

Observation and results: It will be written from observations of the study. At the time of protocol writing analysis is not complete. The expected result of this study is that the group of *Rajanyadi ghrita* shows effective in subsiding the symptom of *Pandu* ,Weakness, Anorexia, Joint pain as well as in objective parameters .

Discussion and Conclusions: It will be drawn from observation and result of study

Scope and Implications of the proposed study: if we get significant result in present study then the further study can be carried out on severe anemia or other Haemopoietic diseases like sickle cell anemia or Thalassemia in children

Ethical consideration:MGACHRC/IEC/October-2020/148

Gantt chart (in Quarterly based, only for long term project, PG and PhD synopsis)

| | | | | | | | | |
|-----------------------|---|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Investigator | Dr Trupti Thakre | | | | | | | |
| Title | Randomized Clinical trial on the efficacy of <i>Dadimadi Ghrita</i> and <i>Rajanyadi Ghrita</i> in <i>Pandu</i> w.s.r. to Iron Deficiency Anemia | | | | | | | |
| Steps | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 |
| Enrolment of Patients | | | | | | | | |

| | | | | | | | |
|------------------------------------|--|--|--|--|--|--|--|
| Medicine preparation | | | | | | | |
| Data collection | | | | | | | |
| Writing thesis parts up to Methods | | | | | | | |
| Data analysis | | | | | | | |
| Writing rest of thesis | | | | | | | |
| Submission | | | | | | | |

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