

Original article

Integration of Ayurvedic formulations with iron folic acid in the treatment of nutritional anaemia among school going adolescents of Dehradun District

Vaidya Balendu Prakash^{1,*}, Shyam Prakash², Rajesh Sharma³, Megha Prakash³, Shikha Prakash³, Kiran Parmar³

¹*Ipca Laboratories Limited, 142-Ab Kandivili Industrial Estate, Kandivili (West), Mumbai, India;* ²*Department of Human Nutrition and Gastroenterology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India;* ³*VCP Cancer Research Foundation, Turner Road, Clement Town, Dehradun, India*

ABSTRACT

Combating anaemia is a global public health challenge of the developing world. Nutritional anaemia is a serious health problem faced by Indian school children. An investigation was taken up to study the effect of non iron containing Ayurvedic preparation *Sootshekhar Rasa* (SR) plus *Sitopaladi Churna* (SC) along with iron and folic acid (IFA) for improving nutritional anaemia among adolescent school going students of Dehradun district in Northern India. The blinded, controlled randomized trial comprised of 820 adolescents anaemic students aged 11 - 18 years. The anaemic students were randomly divided into 4 groups, students of group I (control) received starch, group II, III, and IV students received daily dose of (SR 250 mg + SC 400 mg), IFA and (SR 250 mg + SC 400 mg) + IFA, respectively. All the students received treatment for 90days and were followed up for next 180days. At the end of follow-up (day 270), significant increase of haemoglobin (Hb) level from the base line was recorded in all treatment groups. The maximum gain in Hb concentration was noted in group IV (10.1 ± 0.6 g/L), which was significantly higher than any other group. There were 123 drop-outs; however, no major side effect of treatment was noted in any student. We conclude that daily dose of (SR 250 mg + SC 400 mg) along with IFA can produce sustainable improvement of nutritional anaemia in adolescent students.

Keywords In folic acid, nutritional anaemia, *Sootshekhar Rasa*, *Sitopaladi Churna*

INTRODUCTION

Conditions like anaemia, vitamin A and iodine deficiency continue to pose a major health challenge for growing children and adolescents especially in developing countries like India, even after scientific advances in treatment strategies. In spite of its technical feasibility, the transient methodology of providing supplements with food has not been effective in developing world due to issues with delivery and compliance (Ahluwalia, 2002).

A range of distinctive factors from nutritional deficiencies of iron, Vitamin A, B12 and folate to malaria and chronic inflammatory disorders can cause anaemia (Clark, 2008). However, the most severe consequence of iron depletion is Iron Deficiency Anaemia (IDA).

IDA is a commonly occurring nutritional deficiency worldwide generally arising when body's iron demands are not met due to inadequate intake, impaired absorption or transport, physiologic losses associated with reproductive age, or post disease chronic blood loss (De Maeyer et al., 1989).

Iron deficiency is very common amongst infants and young children that have profound adverse effects on their development patterns (Vijayaraghavan et al., 1990). Nutritional

intake during childhood has a huge impact on a child's present and future health (Kanani et al., 1997). High iron requirement of the body, if not met, makes early childhood one of the highest risk period for iron deficiency (Domellof et al., 2014). Along with causing symptoms such as tachycardia, dizziness, shortness of breath and fatigue, anaemia also leads to cognitive delays and poor achievement scores (Kotecha et al., 2002).

Iron deficiency is a global health issue and prevention or treatment, particularly in children in developing countries, is a major health challenge. Nutritional anaemia adversely affects the mental and physical health of children and also, causes an increase in morbidity. Furthermore, providing iron supplements in later ages may not be effective in combating the effects (Kapil, 2003). A national nutritional anaemia control program was launched to test the effects of iron supplementation in pregnant women, in India, when given after first trimester of pregnancy. The supplementation, however, failed to bring any significant increase in their body's iron content, suggesting that it is important to maintain iron store of a woman before she is pregnant (Deshmukh et al., 2008). Despite all efforts made in this regard, nutritional anaemia continues to be a severely major health issue, suggesting that the efforts have been ineffective.

High prevalence of anaemia has been reported among Indian adolescent girls (Shobha and Sharada, 2003). However, adolescent school children are a neglected group in terms of micronutrients interventions strategies aimed at preschool children or pregnant women (Pollitt et al., 1985). There is not much change as in 2010, the overall prevalence of anaemia was noted to be 32.9% with an increase in incidences in children

*Correspondence: Vaidya Balendu Prakash

E-mail: balenduprakash@gmail.com

Received September 3, 2015; Accepted February 19, 2016; Published February 29, 2016

doi: <http://dx.doi.org/10.5667/tang.2015.0026>

© 2016 by Association of Humanitas Medicine

This is an open access article under the CC BY-NC license.

(<http://creativecommons.org/licenses/by-nc/3.0/>)

Table 1. Various study group and treatment schedule

Groups	No. of Students	Status	Intervention	Dose	Duration (Days)
I.	185	Control Group	Starch	Daily	90
II.	178	Treatment Group	SR + SC*	Daily	90
III.	166	Treatment Group	IFA#	Daily	90
IV.	168	Treatment Group	SR + SC + IFA	Daily	90

*Sootshekhar Rasa 250 mg and Sitopaladi Churna 400 mg, #100 mg of element iron and 500 µg of folic acid.

below the age of 5 years, over a period of 10 years (Kassebaum et al., 2014).

An earlier study with non iron containing Ayurvedic preparations *Sootshekhar Rasa* plus *Sitopaladi Churna* has shown encouraging results in sustaining and improving nutritional anaemia in school going adolescent boys and girls (Acharya, 1935; Prakash et al., 2010). The present investigation was thus initiated to study if combining SR+SC along with iron and folic acid (IFA) produced a better results than SS and IFA given separately in improving nutritional anaemia in school going adolescents.

MATERIALS AND METHODS

Duration of Study

This study was conducted from February to November 2006.

Design

Single blinded, randomized controlled clinical trial: Ethical clearance and permission: the principal and teachers of all the schools involved were given a detailed briefing on the study protocol. Prior permission was taken from the management of all the three schools for conducting this study. This study was approved by State Government of Uttarakhand and a state level committee comprising of experts from Department of Health, Department of AYUSH, Ministry of Health and Department of Education and Administration was formed to approve the study protocol and periodic monitoring of the progress. Free and informed verbal consent of the students and their parents was taken before the start of study.

Analytic Procedures

Haemoglobin estimation was done by cyan meth-haemoglobin method. Internal quality assurance program was carried out periodically for consistency. External quality assurance program was carried out by exchanging samples with laboratory of Department of Human Nutrition and Gastroenterology, All India Institute of Medical Sciences, New Delhi. Anaemia was diagnosed as per WHO recommendation.

Sampling

A total of 1014 school students comprising of 598 girls and 416 boys (11 - 18 years) were initially screened for the study from 8 different schools:

- i) Governments Girls Inter College, Raipur
- ii) Government Inter Collage, Maldevta
- iii) Shiv Junior High School, Maldevta
- iv) Government Junior High School, Miyawala
- v) Doon Higher Secondary School, Shyampur
- vi) Government Girls High school, Raipur and Bahadur Sigh Negi Girls Inter Colle, Gujrada
- vii) Government Junior High School, Gujrara
- viii) Government Junior High School, Chaktunwala.

Total number of anaemic students (n = 820) were then divided randomly into four groups with a specific treatment each. The students were blinded to the treatment assignment.

Ayurvedic Medicines

The Ayurvedic medicines *Sootshekhar Rasa* and *Sitopaladi Churna* were manufactured and provided by Bharat Bhaishajya Shala Pvt Ltd., Dehradun, using modern scientific methods, GMP. These preparations are based on Ayurvedic traditional standards for raw materials, processing and finished products. Raw materials thereby used meet the specifications laid in various traditional texts. The processing of the drug is done in heat furnaces with programmed controls. A particle size analyzer is employed to ensure proper grinding of the medicine and the final end product is monitored by X-Ray Powder Diffractometer for adequate quality control.

Study Design

The study comprised of 820 students. Participating students of group I were given starch and acted as control group. Group II participants received Ayurvedic preparations (SR 250 mg + SC 400 mg), group III received 100 mg elementary iron and 500µg IFA, group IV students received (SR 250 mg + SC 400 mg) along with IFA. On the first day (day 0), blood samples were drawn from all subjects for haemoglobin (Hb) estimation. Thereafter, Hb estimation was done on day 30, 60, 90, 170, and 270 respectively. All the drugs were orally administered as per the schedule given in Table 1.

Compliance

The enrolled students were followed at weekly interval for the treatment period. The field staff visited all the schools regularly to supervise the consumption of the medicines to ensure maximum compliance.

Statistical analysis

The data was analysed by SPSS software (version 12.0, SPSS, Chicago, IL, USA). Mean and 95 percent confidence interval in each group were calculated. A paired test was used to calculate the change in Hb levels within the group. One way ANOVA was used for multiple comparisons among the groups.

Results

Around 80.8% of the total students studied (i.e. 820 out of 1014 students) were found to be anaemic. A total of 78.6% (327) were boys while 82.4% (493) were girls. The haemoglobin concentration of the various intervention groups at different time periods are given in Table 2. At baseline, the mean haemoglobin concentration of various groups was 94.7 ± 12.2 g/L and ranged from 93.9 ± 0.8 g/L to 95.1 ± 0.8 . After 30 days of treatment, significant increase in Hb concentration was

Table 2. Haemoglobin Concentration in g/l (Mean $\pm$ SE) of all groups from baseline to end of study

Groups	No.	Day 0	Day 30	Day 60	Day 90	Day 170	Day 270
Starch	185	95.1 $\pm$ 0.8	94.7 $\pm$ 0.7	94.5 $\pm$ 0.7	95.4 $\pm$ 0.7	94.8 $\pm$ 0.7	94.7 $\pm$ 0.7
SR + SC	178	95.0 $\pm$ 0.9	96.7 $\pm$ 0.7	99.5 $\pm$ 0.7**	101.5 $\pm$ 0.7**	100.6 $\pm$ 0.7**	99.7 $\pm$ 0.7**
IFA	166	94.6 $\pm$ 0.9	95.4 $\pm$ 0.8	97.5 $\pm$ 0.7	97.8 $\pm$ 0.8	97.0 $\pm$ 0.7	96.1 $\pm$ 0.7
SR+SC+IFA	168	93.9 $\pm$ 0.9	98.0 $\pm$ 0.8*	102.6 $\pm$ 0.8**	105.6 $\pm$ 0.7**	105.5 $\pm$ 0.8**	104.1 $\pm$ 0.7**

Differs significantly [$*p < 0.05$; $**p < 0.01$] as compared to control (group I).

observed in group IV. At the end of treatment period, significant differences were noted within and amongst all the treatment groups. Group II (SR 250 mg + SC 400 mg) and group IV (SR + SC + IFA) were found to be better than the group III (IFA). However, the increase in Hb levels in group IV was significantly higher than any other group. At the end of study period (270 days), the mean gain of Hb level (g/L) in the three intervention groups II, III, and IV were 4.6 ± 0.4 , 1.4 ± 0.3 , and 10.1 ± 0.6 g/L, respectively. The maximum gain was noted in the group IV which was significantly higher than any other group. At the end of study period, 123 students dropped out due to various reasons viz. non compliance, parental objection or lost to follow-up. However, no adverse effect of the Ayurvedic medication was recorded in any of the participants.

DISCUSSION

Deficiency of essential micronutrients like vitamin A and iron is very common in Asia. Iron deficiency anaemia affects 40 - 50% of preschool and primary school children (Khor, 2003). A very high prevalence of IDA has also been estimated in adolescents. Literature survey of Srihari et al. indicates that occurrence of anaemia ranges from 19 to 88% across five different cities in India (Srihari et al., 2007). According to a national survey, 79.2% children under 3 years of age and 56.2% of women (aged 15 - 49) have anaemia (Toteja et al., 2006). High prevalence of anaemia (around 80.6%) was seen in adolescent students (Ramachandran P, 1989).

The present study indicated that non iron containing Ayurvedic formulations *Sootshekhar Rasa* and *Sitopaladi Churna* (250 mg + 400 mg) taken daily along with IFA show significant improvement in Hb concentration of students. Participants of both groups treated with SS and IFA also showed significant improvement in Hb levels, however, the maximum gain was observed when SS and IFA were given together. Moreover, a drop in Hb levels was noted in all groups when the therapy was stopped. In an earlier study, SS was found to increase Hb levels significantly in non-pregnant women of reproductive age group (11 - 45 years) (Prakash et al., 2000). Remarkable increase of Hb levels in adolescent students was earlier observed with daily dose of SR 250 mg + SC 400 mg (Prakash et al., 2010). Similar trends were also seen in present study.

A study hypothesis seldom explains the cause of anaemia. In general, iron deficiency results when iron demands of body are not met due to insufficient intake, poor absorption, impaired transport, physiologic losses or chronic blood loss as a result of disease (De Maeyer et al., 1989). Therefore, diet plays an important role in restoring iron deficiency. However, Indian diet predominantly comprises of cereals which are grossly deficient in protective foods. Serious nutritional inadequacies results in low birth weight, retarded growth, and nutritional deficiency (Viteri, 1998). When diet alone cannot restore deficient iron levels to normal within an accepted frame, iron

supplementation has to be provided (De Maeyer et al., 1989). Supplemental iron is available in two forms: ferrous and ferric. Ferrous iron salts are the best absorbed form of iron supplements. Many studies have suggested that a supplement administered twice in a week or even once is as effective as daily supplementation in raising Hb levels (Yip et al., 1988; Yusufji et al., 1973).

In the past, many daily supplementation programs in developing countries have been unsuccessful due to lack of supply and compliance (Galloway and McGuire, 1996). Despite the efficacy and low cost of the ferrous preparations, they are associated with side effects such as nausea, epigastric discomfort, and constipation (De Maeyer et al., 1989). However, in the present study no notable adverse side effects of Ayurvedic for iron were noted in any treatment group.

Iron is a component of every living cell and is essential in the maintenance of health (De Maeyer et al., 1989). It plays a central role in oxygen transport and cellular energy metabolism. The significance of ensuring adequate bio available dietary iron stems from the severe consequences associated with iron deficiency and anaemia, including reduced immune function and resistance to infection, formative delays and irreversible psychological deficiencies in young children, impeded physical work performance, and adverse pregnancy outcomes (Cooper et al., 2006). The quantity of bio available iron is important in diet. This is determined by simulation and inhibitory factors that exist within a meal (Bothwell et al., 1989). Iron supplement should be taken with a source of ascorbic acid such as orange juice as acidic environment facilitates better iron absorption, whereas, food products containing tannins and phytates, such as tea, that reduce iron absorption should be avoided. Also, medicines, such as antacids, proton pump inhibitors, h-blockers, that raise the gastric pH need to be avoided (De Maeyer et al., 1989).

The rationale of using non iron Ayurvedic preparations SS and IFA together was that SS may improve the absorption of iron in gastrointestinal tract. The result from this present study indicates maximum gain of Hb was seen among the participants given SR+SC+IFA. Our present experience and earlier studies indicate that combination of *Sootshekhar Rasa* and *Sitopaladi Churna* may act as catalyst in iron absorption. This Herbo-mineral preparation contains *Bhasmas* of silver, copper, mercury and many medicinal herbs like *Eclipta Alba*, *Cinnamomum zeylanica*, *Zingiber officinale*, *Piper longum*, *Bambusa arumdinaceae*, *Ellettaria cardamomum* and *Cinnamomum cassia* etc. and is described for the treatment of acid refluxes, flatulence, nausea, vomiting, syncope and cough (Sathya et al., 2009). The author of this study observed the synergistic effect of these formulations in improving nutritional anaemia in this clinical practice. Though the consequent control clinical studies establish *prima facie* evidences about the significant improvement of nutritional anaemia by using the stated Ayurvedic formulations, the real strength of Ayurvedic formulations in improving iron deficiency remain largely unknown. There might be many hypothesis or working mechanisms behind the observed effect which need to be explored by designing further experimental and clinical studies.

Adolescence represents a real opportunity to make a difference in life-long patterns (Kaur, 2006). Though there is lot of interest globally in adolescent reproductive health and sexually transmitted diseases, adolescent nutrition has also aroused little interest (Kurz, 1996). Adolescent girls living in developing countries like India constitute a vulnerable group; they get married at an early age and are exposed to greater risk of reproductive morbidity and mortality. However, little attention is given towards the nutritional deficiency in adolescent students. A reason for this inadequate attention may be reluctance to target a new group when even interventions for the primary target group, i.e., pregnant women through prenatal care services, are not functioning adequately. Despite the fact that this pragmatic concern ought not to be taken lightly, it is primarily a logistical supply issue deserving reliable consideration, regardless of additional target group (Kurz and Galloway, 2000). Evidence suggests that control of anaemia in pregnant women may be more easily achieved if satisfactory iron status can be ensured during adolescence (WHO, 1999). To conclude, different causative factors lead to higher incidences of anaemia in developing countries (Tolentino and Friedman, 2007). Nutritional disorders are responsible for most of mortality and drop outs among adolescent students in India (Awate et al., 1997). Evidence suggests that preventive supplements coupled with nutrition education may be a more effective strategy associated with better compliance and improvement of iron status (Ahluwalia, 2002). Our study indicates that there is high prevalence of anaemia in both school going boys and girls. Adolescent health is the most important indicator of development of a nation. Hence, urgent attention is required in this area as proper interventions in school students have shown to improve anaemia.

The result from our study indicates that non iron Ayurvedic preparation *Sootshekhar Rasa* plus *Sitopaladi Churna* given along with IFA rather than only IFA might be a more appropriate combination therapy to improve nutritional anaemia in adolescents. However, further multi-centric studies should be carried to assess the exact potential of this combination.

ACKNOWLEDGEMENTS

The authors are grateful to the then Chief Secretaries Dr. R.S Tolia and Mr. S.K Das, Government of Uttarakhand, for taking the initiative and granting permission to carry out this project. Mr. Premchand Godha of Ipca Laboratories Ltd., Mumbai and Department of AYUSH, Ministry of Health and Family Welfare, Government of Uttarakhand for providing financial support. Dr. G.S Toteja Scientist F, Indian Council for Medical Research, New Delhi, for guidance, study design and arranging collaboration between VCPCRF and All India Institute of Medical Sciences, New Delhi, for ensuring quality control, Department of Health and Education, Government of Uttarakhand for providing requisite logistic support. Principals of the schools giving consent for this study. All field workers and staff of VCPCRF and Mr. Nitin Chandurkar of Ipca laboratories who helped in the drafting of manuscript.

CONFLICT OF INTEREST

The authors have no conflicting financial interests.

REFERENCES

- Acharya JT. Siddha Yoga Sangrah. (Jhansi, India: Baidyanath Bhawan), 1935.
- Ahluwalia N. Intervention strategies for improving iron status of young children and adolescents in India. *Nutr Rev.* 2002;60:S115-S117.
- Awate RV, Ketkar YA, Somaiya PA. Prevalence of nutritional deficiency disorders among rural primary school children (5-15 years). *J Indian Med Assoc.* 1997; 95:410-411, 415.
- Bothwell TH, Baynes RD, MacFarlane BJ, MacPhail AP. Nutritional iron requirements and food iron absorption. *J Intern Med.* 1989;226:357-365.
- Clark SF. Iron deficiency anaemia. *Nutr Clin Pract.* 2008;23:128-241.
- Cooper MJ, Cockell KA, L'Abbé MR. The iron status of Canadian adolescents and adults: current knowledge and practical implications. *Can J Diet Pract Res.* 2006;67:130-138.
- De Maeyer EM, Dallman P, Gurney JM, Hallberg L, Sood SK, Srikanthia SG. Preventing and controlling iron deficiency anaemia through primary health care. Guide for health administration and program managers. Geneva: WHO. 1989;8-9. Available at: http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/9241542497.pdf (accessed on 17th February 2016).
- Deshmukh PR, Garg BS, Bharambe MS. Effectiveness of Weekly Supplementation of Iron to Control Anaemia Among Adolescent Girls of Nashik, Maharashtra, India. *J Health Popul Nutr.* 2008;26:74-78.
- Domellof M, Braegger C, Campoy C, Colomb V, Decsi T, Fewtrell M, Hojsak I, Mihatsch W, Molgaard C, Shamir R, Turck D, Goudoever JV. Iron Requirements of Infants and Toddlers. *J Pediatr Gastroenterol Nutr.* 2014;58:119-129.
- Galloway R, McGuire J. Daily versus weekly: how many iron pills do pregnant women need? *Nutr Rev.* 1996;54:318-323.
- Kanani S, Ghanekar J. Anaemia and adolescent girls: a review of some research evidence and intervention strategies. Department of Food and Nutrition, MS University of Baroda and UNICEF, India, 1997. Available at: <http://www.ijndonline.org/index.php/Ijnd/article/view/46935> (accessed on 17th February 2016).
- Kapil U. Prevention and control of iron deficiency anemia amongst young children. *Indian Pediatr.* 2003;40:293-295.
- Kaur S, Deshmukh PR, Garg BS. Epidemiological correlates of nutritional anemia in adolescent girls of rural wardha. *Indian J Community Med.* 2006;31:255-258.
- Khor GL. Update on the prevalence of malnutrition among children in Asia. *Nepal Med Coll J.* 2003;5:113-122.
- Kotecha PV, Patel RZ, Karkar PD, Nirupam S. Impact evaluation of adolescent girls anaemia reduction programme, Vadodara District, Government Medical College, Vadodara. *Indian J Med Res.* 2009;130:584-589.

- Kurz KM. Adolescent nutritional status in developing countries. *Proc Nutr Soc* 1996; 55:321-331.
- Kurz KM, Galloway R. Improving adolescent iron status before childbearing. *J Nutr*. 2000;130:437S-439S.
- Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, Regan M, Weatherall D, Chou DP, Eisele TP, Flaxman SR, Pullan RL, Brooker SJ, Murray CJ. A systematic analysis of global anemia burden from 1990 to 2010. *Blood*. 2014;123:615-624.
- Pollitt E, Soemantri AG, Yunis F, Scrimshaw NS. Cognitive effect of iron-deficiency anaemia. *Lancet*. 1985;1:158.
- Prakash VB, Pandey S, Singh S. Ayurvedic preparation in the treatment of nutritional anaemia. *Indian J Hemat Blood Trans*. 2000;18:79-83.
- Prakash VB, Prakash S, Sharma R, Pal SK. Sustainable effect of Ayurvedic formulation in the treatment of nutritional anaemia in the adolescence students. *J Altern Complement Med*. 2010;19:211-228.
- Ramachandran P. Nutrition in pregnancy. In *Women and Nutrition in India*. Gopalan C, Kaur S ed. Nutrition Foundation of India. Special Publication Services. pp. 153-193, 1989. Available at: <http://fnb.sagepub.com/content/27/4/311.refs> (accessed on 17th February 2016).
- Sathya T, Murthy B, Vardhini N. Genotoxicity evaluation of certain Bhasmas using micronucleus and comet assays. *Internet J Altern Med*. 2008;7:1.
- Srihari G, Eilander A, Muthayya S, Kurpad AV, Seshadri S. Nutritional status of affluent Indian school children: what and how much do we know? *Indian Pediatr*. 2007;44:204-213.
- Tolentino K, Friedman JF. An update on anemia in less developed countries. *Am J Trop Med Hyg*. 2007;77:44-51.
- Toteja GS, Singh P, Dhillon BS, Saxena BN, Ahmed FU, Singh RP, Prakash B, Vijayaraghavan K, Singh Y, Rauf A, Sarma UC, Gandhi S, Behl L, Mukherjee K, Swami SS, Meru V, Chandra P, Chandrawati, Mohan U. Prevalence of anaemia among pregnant women and adolescent girls in 16 district of India. *Food Nutr Bull*. 2006;27:311-315.
- Vijayaraghavan K, Brahmam GN, Nair KM, Akbar D, Rao NP. ICMR Evaluation of the National Nutritional Anaemia Prophylaxis Programme. *Indian J Pediatr*. 1990;57:183-190.
- Viteri FE. A new concept in the control of iron deficiency: community-based preventive supplement of at-risk groups by the weekly intake of iron supplements. *Biomed Environ Sci*. 1998;11:46-60.
- World Health Organization. Programming for adolescent health and development. Technical Report Series No.886; 1999.
- Yip R, Dallman PR. The roles of inflammation and iron deficiency as cause of anaemia. *Am J Clin Nutr*. 1988;48:1295-1300.
- Yusufji, Mathur VI, Baker SJ. Iron, folate, and vitamin B 12 nutrition in pregnancy: a study of 1000 women from Southern India. *Bull World Health Organ*. 1973; 49:15:22.