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Effect of Hemocare Syrup and Hemocare XT Tablets on Hemoglobin levels in iron deficiency anemia among women of reproductive age: A randomized, placebo controlled, open label trial

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ABSTRACT

Background: Iron deficiency anemia is one of the important public health problems in developing countries among the women of reproductive age group. Hemocare formulation plays a significant role in Iron deficiency anemia because of its Iron content. The present study aimed to investigate the effect of Hemocare Syrup and Hemocare XT Tablets compared with placebo on Hemoglobin Levels in Iron Deficiency Anemia among Women of Reproductive Age.

Methods: A prospective, interventional, randomized, open label, placebo controlled trial has been conducted with 126 patients. Eligible patients randomly received either Placebo 100 mg or Hemocare XT Tablet 100 mg or 10 ml of Hemocare Syrup once daily in the same manner for 4 weeks. Hemoglobin values were documented at the end of 15th day, 21st day and 30th day.

Results: The baseline hemoglobin values were compared with each follow up and statistically significant difference was found at the end of 30th day of Hemocare Syrup and Hemocare XT treatment ($P < 0.05$) but there was no significant difference observed in the placebo group. The study results revealed that 30 days treatment of Hemocare Syrup and Hemocare XT Tablets increases the Hemoglobin levels to 12.46 ± 0.44 g/dl and 12.90 ± 0.98 g/dl from 9.08 ± 2.54 g/dl and 9.68 ± 2.04 g/dl respectively.

Conclusion: Hemocare Syrup and Hemocare XT Tablets treatment showed clinically significant improvement in hemoglobin levels from the baseline and placebo group.

1. Introduction

Anemia is a global problem of immense health significance affecting persons of all ages and economic groups. It has been estimated that 20–30% of the world's population is iron deficient [1]. Iron deficiency anemia (IDA) is the most common type of anemia met with in clinical practice [2]. It occurs at all ages, but is especially common in women of child bearing age, in whom it is an important cause of chronic fatigue and ill health. During the reproductive life of the female, menstruation, pregnancy, parturition and lactation significantly increase the physiological requirements of iron [3]. A recently published study on the burden of disease in India concluded that the burden of IDA is 3.0 times higher than the average globally for other geographies at a similar level of development, and that women are disproportionately affected. The report also highlighted that between 1990 and 2016, the burden of IDA improved little and was the top cause of the years lived with disability (11% of all disability) in 2016 [4].

Hemocare Syrup and Hemocare XT Tablets are used for Iron deficiency due to poor absorption and chronic blood loss, Pregnancy related mineral deficiency, Digestive disorders, Chest pain, Leg pain due to blocked arteries, High blood pressure, Digestive disorder, Heart attack, Mineral deficiencies, Minerals related poor nutrition and other

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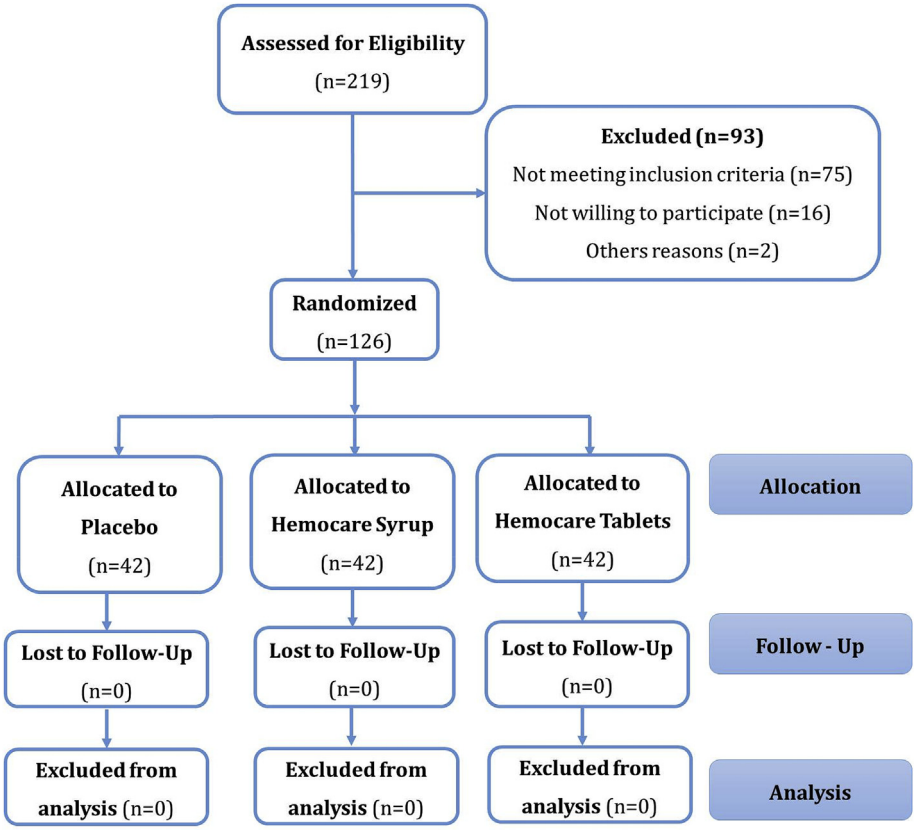

Fig. 1. CONSORT Flowchart

Table 1
Baseline characteristics.

Variable	Placebo (n = 42)	Hemocare Syrup (n = 42)	Hemocare XT Tablets (n = 42)
Age (Years)	38.5 ± 5.36	40.21 ± 2.91	40.88 ± 4.37
Weight (Kg)	58.4 ± 8.42	59.2 ± 8.76	59.8 ± 9.14
Height (cm)	157.6 ± 4.28	158.6 ± 6.25	159.7 ± 5.52
BMI (Kg/m^2)	22.8 ± 3.88	23.4 ± 5.85	23.2 ± 4.28
WC (cm)	94.50 ± 5.24	95.16 ± 3.02	95.57 ± 2.82
HC (cm)	98.42 ± 4.54	100.93 ± 3.07	101.05 ± 3.10
WHR	0.93 ± 0.02	0.94 ± 0.01	0.94 ± 0.015
WtHR	0.61 ± 0.04	0.61 ± 0.03	0.62 ± 0.02
Heart Rate (Beats/min)	71.25 ± 2.94	73.66 ± 2.03	69.42 ± 1.97
SBP (mm Hg)	125.50 ± 12.09	128.47 ± 16.41	127.04 ± 18.59
DBP (mm Hg)	78.95 ± 10.03	77.47 ± 7.85	78.68 ± 13.22
Hb (g/dl)	9.21 ± 2.17	9.08 ± 2.54	9.68 ± 2.04

Values are expressed in mean ± SD, Abbreviations: BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio; WtHR, waist to height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, Hemoglobin.

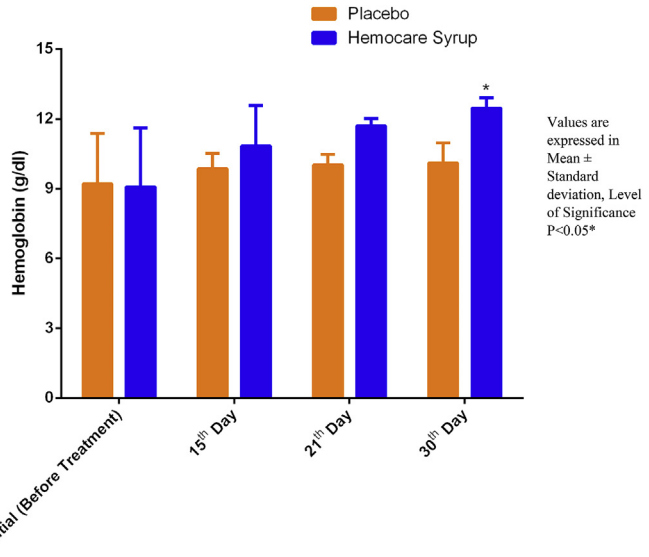

Fig. 2. Effect of Hemocare Syrup on Hemoglobin levels compared with Placebo group in Iron Deficiency Anemia among Women of Reproductive Age
Values are expressed in Mean ± Standard deviation, Level of Significance P < 0.05*.

conditions. The present study was designed to evaluate the Hemocare Syrup and Hemocare XT Tablets in Iron Deficiency Anemia among Women of Reproductive Age.

2. Methods

2.1. Study design and settings

This 4-week, randomized, open label, controlled, parallel-group trial was conducted in the community settings in and around Maraimalai Nagar in association with Urban Health Training Centre (UHTC), Department of Community Medicine, SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology. The institutional human ethics committee approval for the trial protocol was formally obtained from the SRM Medical College Hospital and Research Centre, SRM University Board of Ethics (Grant No: 1344/IEC/2018). This trial was conducted according to the tenets laid down in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to study entry. The participants

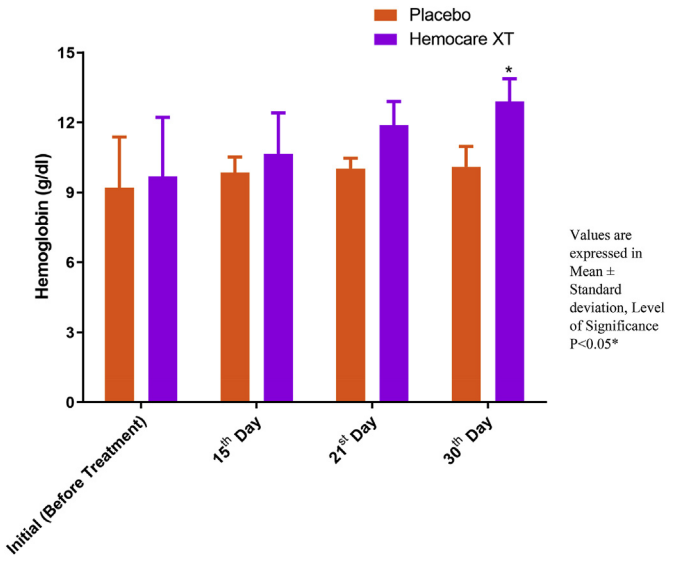

Fig. 3. Effect of Hemocare XT Tablets on Hemoglobin levels compared with Placebo group in Iron Deficiency Anemia among Women of Reproductive Age. Values are expressed in Mean ± Standard deviation, Level of Significance $P < 0.05$*.

were free to withdraw from the study at any time without compromising their relationship with their health care provider. The trial was registered at the clinical trial registry of India (CTRI No:/2018/07/014726).

2.2. Trial participants

Eligible female participants aged 18–45 years who had hemoglobin level < 12 g/dl at the time of inclusion into the study. Exclusion criteria as follows: Hemoglobin < 6 g/dl, IDA with cardiac complications, diabetes mellitus, renal disorder, acute and chronic blood loss, bleeding disorders, hemoglobinopathies, malignancy, pregnancy and lactating women.

2.3. Interventions

Eligible patients randomly received either Placebo 100 mg or Hemocare XT Tablet 100 mg or 10 ml of Hemocare Syrup once daily in the same manner for 4 weeks. Medication adherence was measured using weekly tablet counts/volume of syrup justified against participant reports of medication intake to calculate the proportion of dispensed medication doses that were actually ingested. Hemoglobin values were documented at the end of 15th day, 21st day and 30th day. Any adverse effects of these oral medications were monitored and documented on an adverse effects sheet in the patient folder. CONSORT flow chart was shown in Fig. 1.

2.4. Concealment of allocation

Concealment of the randomization code was done to avoid selection bias. Third party randomization is the gold standard for concealment. Computer generated randomization list was prepared by a third person who was not involved in the recruitment of patients. Each allocation was written on paper and concealed in a serially numbered, opaque envelope.

2.5. Sample size calculation

This pilot study was undertaken to address several process issues before implementation of a full scale randomized clinical trial. The pilot study is essential to plan an adequate full-scale trial because a number of critical issues need to be resolved before time and more significant funding are committed. This study was conducted in a practice-based setting and tested all of the components of a full-scale trial but without the necessary sample size.

2.6. Physical examination

A questionnaire was completed at each health centre by trained interviewers. Demographic information is achieved by a questionnaire. Height and body weight were measured without shoes and with the study subjects wearing light clothes. Height was measured to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg. Measurements were carried out using portable calibrated electronic weighing scale and inflexible measuring bars. BMI was calculated as weight/height^2 (kg/m^2). Subjects were classified into: (i) normal (ii) overweight; (iii) obese, based on a definition of obesity for the population in India. Constant tension tape was used to measure waist circumference (WC) at the midpoint between the inferior costal margin and the highest point of the hip bone across the mid-axillary line, with arms relaxed on the sides. Hip circumference (HC) was measured to the nearest 0.1 cm at the level of the trochanters. Waist to hip (WHR) was calculated as the ratios between their respective components. Blood pressure was measured using a mercury free LCD sphygmomanometer (Diamond, BPDG 234 LCD Super Deluxe); two readings were taken at 10-min intervals after subjects had been seated for at least 10 min. The two readings were averaged. Systolic Blood pressure (SBP) ≥140 mmHg and Diastolic Blood Pressure (DBP) ≥ 90 mmHg consider as high blood pressure.

2.7. Estimation of hemoglobin

A sub-sample of the finger prick blood samples was used to determine the haemoglobin (Hb) level. A calibrated Hemo Control Hemoglobin Analyzer was used to check the hemoglobin levels instantly. This analysis was performed within 5 min of collection.

2.8. Statistical analysis

All the values are expressed as Mean ± SD. One way ANOVA (Dunnett's multiple comparisons test) was used to compare the effect of Hemocare Syrup and Hemocare XT Tablets from baseline to follow up.

Table 2
Multiple comparison test of Hemocare Syrup and Hemocare XT Tablets (Baseline to Follow up).

Multiple Comparison Test	Hemocare Syrup			Hemocare XT Tablet		
	CI	Mean Difference	P Value	CI	Mean Difference	P Value
Initial vs. 15th Day	−12.32 to 9.926	−1.195	0.4256	−4.216 to 2.596	−0.8100	0.2064
Initial vs. 21st Day	−19.75 to 16.31	−1.720	0.4691	−15.34 to 12.32	−1.510	0.4198
Initial vs. 30th Day	27.08 to 22.81	−2.135	0.03104*	25.40 to 21.29	2.055	0.0435*

Values are expressed in Mean ± Standard deviation, Level of Significance $P < 0.05$*.

The minimum level of significance was fixed at $P < 0.05$. Statistical analysis was performed using GraphPad Prism software (Version 6.01).

3. Results

Total 219 subjects were assessed for eligibility, in which 93 subjects were excluded because of unwillingness and didn't meet to inclusion criteria. Rest of 126 participants was randomly assigned into three groups. Group A, B and C received Placebo 100 mg OD, Hemocare Syrup 10 ml OD and Hemocare XT 100 mg OD respectively (Fig. 1). Baseline characteristics of the treatment groups were shown in Table 1. One way ANOVA was used to compare the baseline characteristics among the groups but no significant difference was found at baseline.

Hemoglobin levels of Placebo, Hemocare Syrup and Hemocare XT group before treatment were found to be 9.21 ± 2.17, 9.08 ± 2.54 and 9.68 ± 2.04 g/dl respectively. There was no significant difference among placebo, Hemocare syrup and Hemocare XT groups on hemoglobin levels at initial stage. After treatment, the changes in the hemoglobin values were documented at the end of 15th day, 21st day and 30th day. The initial hemoglobin values were compared with each follow up and statistically significant difference was found at the end of 30th day of Hemocare Syrup and Hemocare XT treatment ($P < 0.05$) but there was no significant difference observed in the placebo group. (Figs. 2 and 3). Multiple comparison test was carried out to compare the baseline hemoglobin values with each follow up (Table 2).

The study results revealed that 30 days treatment of Hemocare Syrup and Hemocare XT Tablets increases the Hemoglobin levels to 12.46 ± 0.44 g/dl and 12.90 ± 0.98 g/dl from 9.08 ± 2.54 g/dl and 9.68 ± 2.04 g/dl respectively.

Safety and tolerability of drugs were assessed by physical examination including Blood pressure and heart rate. No patient had withdrawn their consent from the study due to adverse drug reactions.

4. Discussion

The World Health Organization (WHO) has estimated that half of anemia cases are due to iron deficiency. Iron deficiency boosts healthcare costs worldwide, hinders learning ability in school children, and reduces adult productivity; although prevention is relatively low cost [5]. Ferrous sulfate is the most common iron supplement but it carries a major risk of noncompliance due to side effects if it administered directly [6]. Here we compared the efficacy and safety of popular Hemocare formulations with placebo in Iron Deficiency Anemia among Women of Reproductive Age.

In our study, at the end of 30 days, the mean hemoglobin level was increased in the patients treated with Hemocare Syrup and Hemocare XT Tablets from their respective baseline values, as compared with Placebo. A similar kind of results were obtained from the study conducted by Geetha et al., 2014 [7] where iron supplement improves the mean hemoglobin level.

A study conducted in Gujarat among adolescent girls, reported 21.5% and 10.3% reduction in the prevalence of anemia and serum ferritin deficiency respectively, following 17 months of weekly IFA (Iron + Folic acid) supplementation with a mean rise of hemoglobin levels to 6.4 g/dl [8]. One more long-term study among school and non-school going adolescent girls in Lucknow, Uttar Pradesh, reported 48% reduction in the prevalence of anemia after 4 years of weekly supplementation of IFA, family life education and deworming with an increase in hemoglobin levels from 10.8 to 11.8 g/dl [9] because hookworm infection is an important cause of iron deficiency anemia, especially more severe anemia. Similarly in the present study we have used Albendazole (400 mg) for deworming and 30 days of Hemocare Syrup and Hemocare XT Tablets treatment increases the Hemoglobin levels to 2.2 g/dl (mean rise) from the baseline.

The main limitations of our study include its small sample size, and the relatively well-controlled population enrolled in the study based on Hemoglobin levels alone. One more limitation of the study was the inability to blind the investigators to study drug due to the different dosage forms and dosing regimens of each drug.

In conclusion, Hemocare Syrup and Hemocare XT Tablets treatment showed clinically significant improvement in hemoglobin levels from the baseline ($p < 0.05$). It is our hope that this preliminary data will be utilized to design large-scale longer-term trials with similar objectives in Iron Deficiency Anemia among Women of Reproductive Age.

Conflicts of interest

The authors declare that none of them has any conflict of interests.

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