Alternative treatment for iron deficiency anemia: Irocbin versus sherbat Faulad

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Abstract: The widespread reason of anemia is Iron deficiency in Pakistan and even worldwide. A clinical trial was undertaken to assess the efficacy of Irocbin formulation for the treatment of iron deficiency anemia as compared to Sherbat Faulad. The curative evaluations of these medicines were recorded in clinically and biochemically identified cases of iron deficiency anemia. The therapeutic evaluation of the different drugs both test and control drug were conducted on the bases of improvement in the subjective signs and symptoms, clinical observations and biochemical investigations at periodic intervals during the course of therapy. This data was collected in the period November 2010 to November 2012 and completed the clinical trials. According to the statistical analysis comparison of data recorded by patients concerning to different variables, showed significant results between test and control groups (p<0.05). By applying ANOVA test, the p values for multiple comparisons of the levels of improvement of Hemoglobin after treatment exhibited significant difference as compared Sherbat Faulad and Irocbin. The control drug Sherbat Faulad with only iron component improves Hemoglobin level and the sign and symptoms but associated with side adverse effects.

Keywords: Iron deficiency anemia, Irocbin, Sharbat Faulad, efficacy

INTRODUCTION

Low iron level is one of the most addressable issues in developing countries globally. Women and children are affected more than males (Yip, 1997). A thorough literature survey of prevalence studies demonstrated that all those suffering from any bleeding disorder are at most risk as compared to other population especially pregnant, lactating females, growing children and elderly people with some underlying disease (Wintrobs, 1993). Anaemia is a clinical condition occurring due to low hemoglobin concentration in blood. The normal percentage of hemoglobin varies with subject to age, sex, physiological condition and altitude of any person (Viteri, 1998). Iron deficiency affects 30% of the world’s population which is equal to 500 million peoples. This is high fig evidenced by the reason that the human body holds a limited ability to absorb iron from the GIT and the frequent loss of iron as result of hemorrhage from the body. Normally there is abundant iron in the body and most of it is available in insoluble form as a ferric Fe+++ form, which carries poor bioavailability. Ferrous Fe++ form is easily absorbed. Free iron is toxic and reason that it is bound to specific proteins, which helps in the transport and storage of iron in the body (Kumar et al., 2005).

The exact clinical manifestation of this condition varies patients to patients; it also depends upon the severity of iron deficiency status. The major clinical findings reported as generalized weakness, difficulty in concentration, fatigue and exercise intolerance. Furthermore it may be asymptomatic. Other less reported clinical reporting’s including alopecia, atrophy of lingual papillae, or dry mouth. This is might be due to the deficiency of iron enzymes present in epithelia and the gastrointestinal tract.

There might be no Physical signs or pallor skin or conjunctiva depending upon the severity. In severe case systolic murmur and abdominal and rectal exploration might be present (Rector, 1989). The first line of treatment of anemic patients is to restore hemoglobin besides controlling iron loss and to evaluate the actual cause. The target is got by treatment with ferrous sulphate 200 mg b.d. Small doses are more effective and well absorbed and tolerated. Other iron preparations such as ferrous fumarate, ferrous gluconate or formulations containing iron suspensions may also be accepted superior then ferrous sulphate. Ascorbic acid (250-500 mg twice daily with the iron preparation) may improve iron absorption. The oral iron is continued until three months after the iron deficiency has been corrected so that stores are replenished [Hallberg et al., 1987; Fishbane, 2003).

Methodology

The is was a clinical trial of test herbal formulation coded such as Irocbin, and another herbal proprietary product Sherbat Faulad (Hamdard), which were utilized for the cure of iron deficiency anemia. In this research-based study subjects were randomly allocated either one of the test herbal medicine or control herbal medicine. Clinical history, physical and biochemical examination of the registered patients at the base line were recorded and were monitored on each follow up.

This was a case control, observational, multicenter evaluation based study, conducted on the patients living in...
the Gadap Town adjacent Madinat-al-Hikmah, Hamdard University, Karachi. They patients were registered either at Shifa-ul-Mulk Memorial Hospital, Karachi, Amna Unani Hospital, or Brooks Health Care Centre Surjani Town; all hospitals are located in the Gadap Town, Karachi. The patients were registered and thereafter follow up was carried from November 2010 to November 2012.

The study was conducted according to the standard of good clinical practices and a prior ethical approval was taken from Ethical committee, Hamdard University. Data were collected on clinical trial proforma and was analyzed on SPSS.

**Diagnostic technique**
Patients were examined clinically and the patients having the sign and symptoms of iron deficiency anaemia were enrolled in the study. Clinical evaluation proforma was filled up before starting the treatment at baseline and the clinical record was continuously updated during the course of the treatment at every scheduled visit of the patient. Proforma was designed on the bases of clinical evaluation and assessment of improvement. Further diagnosis of iron deficiency anaemia was determined on the basis of blood Hemoglobin (Hb), packed cell volume (PCV), Red blood cells count (RBC), Mean Corpuscular Volume (MCV), Mean corpuscular hemoglobin concentration (MCHC), Mean corpuscular Hemoglobin (MCH), and serum Ferritin level which are considered as gold standard test for the diagnosis and base line confirmation of iron deficiency anaemia.

**Test drugs**
Irocbin, were prescribed to test groups and Sherbat Faulad (Hamdard) were administered to control group for 04 weeks in a random manner. Detailed history and clinical examination was done as per the clinical trial proforma designed for this study. The patients were advised to note down the incidence and severity of symptoms during the course of treatment. Side effects were noted by the physician monitoring the patients enrolled for the study.

**Data collection**
The complete record of patient’s data was taken on clinical trial protocol proforma, in which all the related complaints were recorded.

**Inclusion criteria**
Following criteria was followed.
- Iron deficiency anaemia patients.
- Patients residing in Gadap Town Karachi.
- No other disease that mimic Iron deficiency anaemia.
- All socioeconomic groups were included.
- Cases of 05 to 60 years of age.

**Exclusion criteria**
- The major exclusion criteria for this trial were:
  - Patients belonging to the distant area outside Karachi were excluded because of inherent difficulty in follow up.
  - Unstable angina.
  - Uncompensated Congestive cardiac failure (CHF).
  - Poorly controlled arrhythmia;
  - Uncontrolled hypertension [>150/95 mm Hg].
  - Dialysis.
  - History of solid organ transplantation.
  - Hemochromatosis.
  - Hemolytic anemia.
  - Haemosiderosis.
  - Patients with a history of drug abuse and those with known poor compliance were excluded.
  - Patient having history of adverse reaction to any of the study drugs as or contraindicated for their use.

**Dosage form design**
At the outset a test herbal formulation was designed to treat iron deficiency anaemia and in turn was compared with control herbal drug Sherbat Faulad (Hamdard). The designed test herbal formulation as conceived was designated as Irocbin.

The identity of the herbal specimens were authenticated by Prof. Dr Iqbal Azhar, Chairman Department of Pharmacognosy, University of Karachi and all the crude drugs specimens have been deposited in the Meteria Medica Museum of the Faculty of Eastern Medicine, Hamdard University Karachi, and tagged numbers were allotted (Table 1) and mentioned. The coded test and
control drugs were enumerated with authentic botanical nomenclature local or vernacular names and quantity used.

**Irocbin**
All the plant material, *Rosa damascena* Mill. (Gul-e-Surkh) 50mg/5ml, *Zizyphus jujuba* Mill. (Unab) 50mg/5ml, *Elettaria cardamomum* (L.) Maton. (Ilaichi) 50mg/5ml, *Prunus armeniaca* Linn. (Khobani) 50mg/5ml, *Prunus domestica* Linn. (Aloo Bukhara) 50mg/5ml, *Punica granatum* Linn. (Anar dana) 75mg/5ml, *Phyllanthus emblica* Linn. (Amla) 50mg/5ml, were first cleaned and dirt was completely removed. Then the drugs were either cut down into small pieces or crushed under the machine to make powder, and then the weighed dry herbs were boiled in water for about 2 hours till the quantity of the aqueous extract was reduced to half of its original quantity added. There after the aqueous extract so obtained was filtered with Whatman filter paper no 60, then sugar was added to it, again it was boiled for 10 to 15 minutes. During the process of mixing sugar with aqueous phase, the foam so appeared in the mean while, was continuously removed. To the syrup so obtained, Sodium benzoate 1gm/Kg was added as a preservative. It was then cooled down and filled in bottles of 120ml each with machine. These filled bottled were then sealed and labeled as Irocbin. Properties and ingredients shown in table 2.

**Composition**
A batch of 10 liters, Irocbin Liquid: Each 5ml contains:

**Indications**
Iron deficiency anaemia, Prophylaxis and treatment of iron deficiency anaemia, Promotes haematopoiesis, lack of appetite & growth.

**Dosage forms:** Syrup, Pharmaco-therapeutic group: Hematinic.

**Pack Size:** 120ml bottle

**Excipients:** Sugar, Sodium benzoate, orange Flavor

**Contraindications**
Hemochromatosis, Hemolytic anaemia, Haemosiderosis. Hypersensitivity to any of the ingredients.

**Dose**
For adults its dose for Treatment was given as 2-3 tea spoons a day in divided doses. For Prevention: 2 tea spoon a day. For Children having age between 6-12 years its dose in treatment for Children weighing over 22kg: one tea spoon a day. Children weighing over 44kg: one tea spoon twice a day. Children weighing over 66kg: one teaspoon three times a day.

**Side effects:** No side effects reported

**Precautions:** Do not use without the advice of Physician during pregnancy. Diabetic patients should not use it as it contains sugar.

**Storage conditions:** Store in a cool and dry place below 25C. Keep all medicines out of reach of children. **Validity period:** 3 years, do not use after the expiry date mentioned on the pack.

**Presentation:** Safely sealed bottles of 120 ml together with instructions

**Interactions with other drugs:** Not established

**Overdose:** No case of overdose has been reported so far.

**Sherbat faulad (Hamdard)**
Sherbat Faulad is the proprietary product of Hamdard laboratories (Waqf) Pakistan to treat iron deficiency anaemia. Sherbat Faulad is helpful in the growth of children and beneficial for anemia. It can be used by the persons of all ages and in all seasons. It increases the academic performance of students. It gives energy to the liver. It is an effective tonic for females especially during pregnancy and lactation. It improves functioning of liver. Helps in developing resistance against weakness and diseases.

**Side effects**
Not reported.

**Composition**
- Iron compound
- Strychnos nux vomica (Azaraki-Treated)
- Sucrose
- Food color
- Preservatives

**Packing**
Syrup: 120 ml packing.

**Dosage:** Should be used by physician advice in following ways:
- In adults 2 tsp twice a day.
- In children 1 tsp twice a day.

**Note:** Kept in a cool and dry place.

**Tests and duration of the treatment**
**Total duration of treatment:** 4 weeks (one month)
**Hematological parameters were:** Hemoglobin level (HB %), Mean corpuscular volume (MCV), Mean corpuscular Hemoglobin concentration (MCHC), and Serum ferritin level.

**Measurement before start of treatment:** At the baseline
**Measurement at the end of treatment:** At the end one month (4 weeks)

**Normal values of RBC:**
- **Total RBC Normal count:** Male: 4-5 million/cmm, Female: 3.5- 4.5 million/cmm
- **Hemoglobin Normal:** Male: 14-18 gms%. Female: 12-16 gms%
Hematocrit (Packed Cell Volume) (PCV) Normal: Male: 40-50%. Female: 37-47%.
ESR Normal: Male: 0-10mm/hr, Female: 5 -15 mm/hr.

**Physical examination**

Anaemia produces non-specific pallor of the mucous membrane. A number of abnormalities of epithelial tissues are described in association with iron deficiency anaemia. These include esophageal webbing, koilonychia, glossitis, angular stomatitis and gastric atrophy. The exact relationship of these epithelial abnormalities to iron deficiency anaemia is unclear and may involve other factors. For example, in a report published in United Kingdom, it was cited that 15% of the patients with iron deficiency anaemia were suffering from atrophic changes in mouth and angles of the mouth, but comparatively this fig. is much less in U.K as compared to underdeveloped countries. In severe, untreated and chronic of Iron deficiency anaemia, patients may also suffer from splenomegaly.

**RESULTS**

Anemia is a condition in which not enough red blood cells are being produced in body resulting in poor distribution of oxygen to organs. A person or patient who is suffering from anemia experiences fatigue, constipation problem, cold hands and feet, headaches and possibly fast or irregular heart beat. Iron deficiency anemia occurs when the body does not store enough iron or cannot absorb enough iron to help build red blood cells. In addition taking iron supplements or herbal supplements that contain large quantities of iron can be dangerous if you do not need additional iron in your dietary schedule.

The literature search on the plants has been selected on the bases of their test drug Irocbin, and Sherbat Faulad. The medicinal plants and their parts utilization as a component of products of natural medicine are being used for iron deficiency anemia are very well documented in ethno medical study beside being given in the Unani pharmacopeia and Qarabadins. The Irocbin contain *Rosa damascena, Zizyphus jujuba, Elettaria Cardamomum, Prunus armeniaca, Prunus domestica, Punica granatum and Phyllanthus emblica* see table 3.

The details of these ingredients, the dosage from design prescribed, precaution, storage condition validity period, presentation, interaction with the drugs and other details are provided in detail in methodology section. The detail composition of Sherbat Faulad and test drug Irocbin is also given in methodology section so as to high-light the salient features of their components and constituents. The drug Irocbin was designated as test drug; whereas Sherbat Faulad was designated as control drug. These test and control drugs were treated in the statistical parameters.

**Serum ferritin level**

Level of serum ferritin was measured and compared by using ANOVA in both groups of treatment before and after treatment. It was recorded that control drug Sherbat Faulad is more significant ($p<0.05$) to improve the level of serum ferritin as compared to Test drug Irocbin as shown in table 4.

![Graph 1: Improvement in symptoms by Irocbin (Test drug)](image1)

![Graph 2: Improvement in symptoms by Sherbat Faulad (Control drug)](image2)

**Improvement in clinical features**

The most common clinical features associated with anemia are breathlessness, tachycardia, poor appetite, easy fatigue, headache, irritability dizziness and general weakness etc. All the clinical features were noted before and after treatment and comparative analysis was done at the end of treatment. Multiple comparisons of two groups were done by using ANOVA and statistically significant improvement was noted in both groups after treatment as shown in table 5. It is concluded that both drugs have significant importance to reduce the clinical symptoms related to anemia. Therefore it can be deduced from the $p$ values afforded for sign and symptoms, the test drug Irocbin and control drug Sherbat Faulad improves the sign and symptoms well, which may be due to the nutritional component in case of test drug along with iron contents while the control drug Sherbat Faulad with only iron component improves the sign and symptoms but associated with side adverse effects.
Improvement in intensity of clinical features calculated by Wilcoxon signed rank test

Intensity of symptoms is the parameter to record the level of improvement. In this study, intensity of symptoms was recorded as absent: 1, mild: 2, moderate: 3 and severe: 4 at baseline (T0) and after the completion of treatment (T1). Median values, interquartile ranges (IQR) were determined and p values were calculated by using Wilcoxon signed-rank test to record the indirect effects of both groups in the improvement of Hb level and clinical features associated with anemia.

Improvement in intensity of clinical features by test drug

Irocbin (Test drug) showed significant improvement in all symptoms associated with anemia analyzed by Wilcoxon signed rank test as shown in Table 4 and graph 1.
Improvement in intensity of clinical features by control drug

Level of improvement by control drug was measured by Wilcoxon signed rank test is shown in Table 7 and graph 2.

The objective of this study was to compare herbal coded formulation comprising of different medicinal plants with control drug available in the market to see whether these may represent a platform for the development of novel therapeutics.

Adverse effects

The adverse effects were very carefully observed in both the test and control groups. There were no adverse effects reported by the patients of the test drug, as it may be due to the reason that the test drugs contain purely natural ingredients and have no synthetic elements which further endorse the fact that naturally ingredients always suits best to the health, so patients of test group indicated good compliance in relation to drug acceptability. Some patients of the control group reported gastric irritability,
nausea and constipation, which may be due the presence of ferrous sulphate resulting poor patient compliance. In conditions of treatment failure, adverse reactions, patients were given alternative treatment at the Shifa Ul Mulk Memorial Hospital, Hamdard University, Karachi, Amna Unani Hospital, and Brookes Health Care System, Surjani Town, Karachi with full care throughout the end.

DISCUSSION

Iron deficiency anemia is a blood disorder in which the number of oxygen carrying red blood cells in the body decreases. Typically anemia occurs due to insufficient iron supply that causes the iron in the bone marrow to deplete. Next, the iron deficiency begins to affect hemoglobin production until it declines significantly. When this occurs the anemic body shows symptoms such as dizziness, fatigue, pale skin, weakness, rapid or irregular heartbeat, memory loss, confusion, breathlessness, irritability and headaches. The objective of this research was to characterize iron deficiency with the use of herbal and iron elements. For this purpose two different dosage form design consisting of test drug Irocbin, and control drug Sherbat Faulad (Hamdard) were used to assess their efficacy in Iron deficiency anemia. This test and control drugs were administered to two groups of patients registered on the bases of inclusion and exclusion criterion parameters. Thereafter preliminary screening of Hb analysis, these drugs were prescribed and administered for 30 days and further window period of 30 days so as to assess the compliance of effectiveness of the mode of treatment. The diagnosis of anemia was determined on the evaluation of hematocrit and hemoglobin level and efficacy examined on achieving the normal level of these values.

The data so generated on two different dosage forms were analyzed through statistical parameters. Multiple comparison of level of improvement of hemoglobin in treatment groups before and after treatment in test and control groups were quantified and assessed on mean difference, confidence intervals along with both lower and upper mark. The serum ferritin level by comparing with one-way Anova was analyzed where in improvement and progress was noted. In the similar manner the sign and symptoms recorded was also subjected with one-way Anova and extended by Tukey HSD analysis, significance displayed the efficacy. These parameters were breathlessness, tachycardia, poor appetite, headache, fatigue and general weakness. Improvement in the intensity of clinical features calculated by Wilcoxon signed rank sum test. The results so obtained clearly displayed that mark improvement was statistically observed with control drug Sherbat Faulud as compared to test group. However the test drug Irocbin did not respond well to increase the hemoglobin and other biochemical parameters, but Sherbat Faulud effects were quite visible. The control drug Sherbat Faulud as compared to Irocbin was quite promising in improving the hemoglobin contents and improvements in sign and symptoms, but their adverse showed the intolerance.

CONCLUSION

Therefore it can be deduced from the p values afforded for sign and symptoms, all the test drug Irocbin, syrup and Sherbat Faulud improves the sign and symptoms well, which may be due to the nutritional component in case of test drug along with iron contents while the control drugs Iberet and Sherbat Faulud with only iron component improves the sign and symptoms but associated with side adverse effects.

ACKNNOLEDMENTS

Sherbat Faulud was kindly supplied by Mr. Ubaidullah khan, Director Production, Hamdard Laboratories, Waqf, Pakistan. The total quantity supplied as 15 liters on June 6, 2012.

REFERENCES


