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ORIGINAL ARTICLE

A Randomized Control Study to Evaluate Effects of Short-term Oral Iron Supplementation in Regular Voluntary Blood Donors

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Abstract Regular blood donation can lead to iron deficiency anaemia. Early recognition and reversal of excessive iron loss by iron supplementation may avoid symptomatic iron store depletion in blood donors. The aim of this study was to assess the efficacy of iron supplementation in maintaining the iron stores of voluntary blood donors. A total of 200 regular volunteers who donated twice in previous year were randomly divided into two groups. Iron: oral iron supplementation tablets of elemental iron as ferrous fumarate. Placebo group: glucose containing capsules, to be taken once daily for 21 days after one unit of blood donation. Their hemogram, serum ferritin, red cell indices and red cell distribution width were determined at baseline and after 1 month and at the time of next blood donation. Out of 200 volunteers enrolled 98 were assigned to iron group and rest 102 into placebo group. Total of 37 % donors dropped out, yielding a dropout rate of 35 % in iron group and 39 % in the placebo group. The haemoglobin and ferritin levels showed significant improvement in iron group compared to placebo group ($p < 0.05$). Three weeks of oral iron therapy (98.6 mg elemental iron/day) was able to maintain iron stores at 1 month after donation but was not sufficient to sustain the iron stores over a period of 3 months. Thus there is need to evaluate increased dosage or duration of iron supplementation in maintaining the iron stores.

Keywords Voluntary donors · Iron · Hemoglobin · Serum Ferritin

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Introduction

Anaemia is the most common nutritional deficiency disorder in the world [1]. Iron deficiency anaemia (IDA), the most frequent form of anaemia, is defined as a haemoglobin (Hb) level <130 g/l in men and <120 g/l in women in the presence of depleted iron stores [1]. Prevalence in India is 65–75 % [2]. Important causes of IDA are poor diet, gastrointestinal blood loss, malabsorption, parasitic infestation, but there is one cause that is recognized but always under viewed and that is repeated blood donation. In India, healthy individuals can donate blood up to four times a year (at three monthly intervals) [3]. A donor generally donates approximately 450/350 ml blood at the time of donation resulting in loss of approximately 225/175 mg of iron. This volume of blood to be collected is decided on the basis of donor weight (350 ml for <60 kg and 450 ml for >60 kg weight) as per our departmental standard operating procedure. Repeat regular whole-blood donors show lower serum ferritin levels than first-time donors. Thus a large number of regular blood donors develop negative iron balance that may eventually progress to IDA leading to potential loss of considerable number of regular blood donors who actually represents the best source of safe blood.

In a previous study from the region, Mittal and coworkers [4] have demonstrated that as high 49 % of male and 100 % female donors donating blood thrice a year, while 24 % of males and 27 % female donors donating blood only twice a year were iron depleted (serum ferritin <15 ng/ml) [5]. At our centre approximate annual blood collection is 55,000 units out of which 83 % is contributed by voluntary blood donors (VBD). Of these 49 % are regular and repeat VBD. These blood donors are at risk of being anaemic due to depletion of their iron stores.

To address this problem of iron deficiency in blood donors either we need to limit donation frequency or to provide iron supplementation. Limiting donation frequency has the disadvantage of reducing the already scarce blood supply. Iron supplementation seems to be a better option to prevent iron depletion and its effects in blood donors. However, iron administration is associated with considerable gastrointestinal side effects and may result in diminished compliance in otherwise asymptomatic blood donors. Iron administration and dosage regimens need to be optimised in regular blood donors. In the present study conducted at our institute we have assessed haematological parameters and serum ferritin levels in regular blood donors after administration of oral iron for 3 weeks post donation.

Materials and Methods

Study Design

The design was a prospective, single blinded, longitudinal intervention study with the randomization of repeat, regular, non-remunerated, VBD into two groups. The study was approved by the ethics committee of the Institute and the blood donors were selected as per the criteria laid down in the Drugs and Cosmetics Act and Rules, Ministry of Health and Family Welfare, Government of India. Hemoglobin (Hb) was estimated at the time of donor screening by digital photometric device (HemoControl—Haemoglobin photometer EKF diagnostic GmbH, Barleben Germany).

Inclusion criteria were at least two blood donations in the last 1 year, Hb $\geq$12.5 g/dl with screening test and willingness to return for the follow up visits, while the volunteers giving history of hypersensitivity to iron or side effects to previously administered iron therapy were excluded from the study. Donors already on iron supplements were also excluded. The cut-off value of Hb of 12.5 g/dl was same in both males and females as per the national regulations [3]. Selected participants were enrolled in the study after obtaining a written informed consent and were randomized into two groups: Iron and Placebo group respectively. Each donor in Iron group was given 21 doses of 300 mg ferrous fumarate (equivalent to 98.6 mg elemental iron) while other group received glucose containing capsules identical to ferrous fumarate capsules as a placebo to be taken once daily for 21 days.

Sampling and Follow-Up Visits

Each volunteer donor was scheduled for a total of three visits: an initial visit (visit 1) on Day 0, the second (visit 2) after 1 month (after completion of oral iron therapy) and third (visit 3) at the time of next blood donation (3-6 months interval).

Pre donation 8 ml blood sample was taken (5 ml in plain and 3 ml in EDTA vacutainer) to assess pre-donation baseline serum ferritin and haematological parameters. Routine screening for Hb was based on finger prick capillary samples and Hemocontrol device. Iron or placebo supplementation was given to each donor, as per the randomization. 2nd blood sample was taken after 1 month of donation to see the trend in iron status after giving iron supplementation. Side effects and compliance were assessed. 3rd blood sample was taken after interval of 3–6 months, whenever the donor returned for repeat donation, to study the stability of iron status in both groups after supplementation (Fig. 1).

Parameters Assessed

Demographic details including age (years), weight (kg), dietary habits, age at first blood donation were noted while donation profile which includes total previous cumulative donations, donations in last 1 year and interval between donations were also assessed.

Laboratory Investigations

Venous blood sample collected in EDTA vacutainer was processed on the same day of collection for estimation of Hb, Hematocrit, Red cell indices (MCV, MCH and

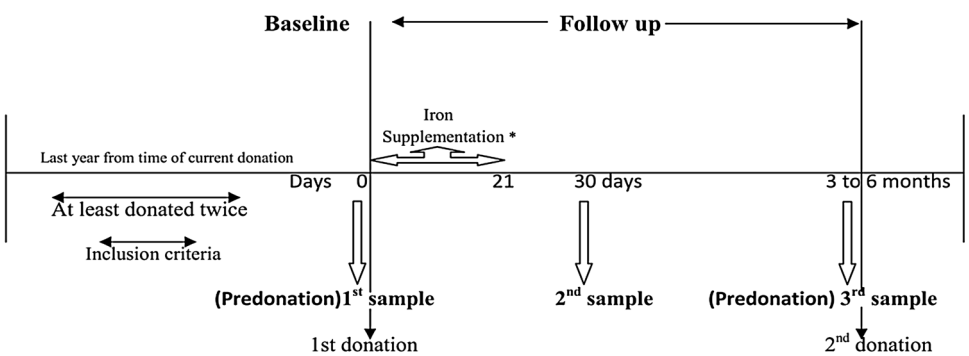

Fig. 1 Schedule of sampling

MCHC), RBC count and RDW by automated cell counter (KX21, Sysmex Corporation, Kobe Japan) while from plain vacutainer serum was separated and stored at −80 °C deep freezer. Serum ferritin was estimated in batches with commercial enzyme linked immunosorbent assay (ELISA) kits (DIAMETRA, Italy). In this study, iron stores were considered depleted at serum ferritin values <15 ng/ml, reduced at values between 15–30 ng/ml, and normal or replete at values from 31 to 300 ng/ml.

Statistical Analysis

Sample size was estimated to be 70 donors in each group by using PASS software version 3.0.43. However considering the approximate dropout rate of 30–40 % as per the literature reviewed, we included 100 subjects in each group. SPSS 20.0, Inc. Chicago, IL was used for data analysis and calculations. Skewness was calculated to assess the normal distribution of data and non-parametric test (Mann–Whitney test, Kruskal–Wallis test and Wilcoxon signed ranks test) was used for serum ferritin, hematocrit and total previous donations. Independent sample *t* test was used to compare the mean values among the two groups. Paired t-test was used to compare mean values at visit 1, visit 2 and the final visit for each group. All tests were two-tailed and a p value of less than 0.05 was considered significant.

Results

Donor Selection and Follow-Up

Total of 3623 regular non remunerated VBD donated blood in 20 blood donations camps during the study period (December 2011–August 2012), of these 371 donors had the history of at least 2 donations in previous year, 157 out of 371 donors declined to participate in the study (Fig. 2) and 14 donors did not meet the inclusion criteria (Fig. 2). Thus, total 200 donors were included in the study and were randomly divided into two groups Iron (n = 98) and Placebo (n = 102). Out of this 72 donors returned for 2nd visit in the iron group yielding a dropout rate of 26 %, while for placebo 71 donors returned yielding a dropout rate of 30 %. For 3rd visit 64 and 62 donors returned in respective groups. Dropout rate during the study was more than expected considering the estimated sample size. Reasons for drop outs are provided in Fig. 2. The mean interval between the visit 1 and visit 2 was 33.4 days while between visit 1 and visit 3 was 3.5 months.

The baseline parameters were similar in both groups except for differences in the total number of previous donations and the hematocrit values (Table 1).

Although routine screening for Hb based on finger prick capillary samples and Hemocontrol device showed that all 200 donors had an initial acceptable Hb but while testing on venipuncture sample by haematology analyzer Hb values <12.5 g/dl were seen in 57 (28.5 %) donors. The mean serum ferritin value was normal but serum ferritin level <15 ng/ml was recorded in 61 (30.5 %) donors. When mean serum ferritin levels were compared with annual blood donation frequency it was observed that mean serum ferritin (27.8 ng/ml), MCV (84.64 fl) and MCH (26.84 fl) was found to be lower in donors who donated 4 times in 1 year compared to those who donated blood twice in a year mean serum ferritin 48.1 ng/ml, MCV (88.63 fl) and MCH (28.79 fl) respectively. This data shows statistical significance ($p < 0.05$) in relation to annual donation frequency and alteration in iron status (Fig. 3).

Effect of Iron Supplementation

Of the 200 donors enrolled in the study only 126 donors completed all the three visits. Mean values on visits 1, 2 and 3 for both the groups are shown in Table 2.

In the iron group, Hb increased from 12.9 gm/dl to 13.8 gm/dl i.e. mean rise of 0.9 gm/dl, which remained nearly constant (13.7 gm/dl) at the next donation interval (visit 3). Hematocrit showed increase of 3.2 % at visit 2 which was maintained till next visit. RBC count showed a rise from $4.6 \times 10^6/\mu L$ to $5.0 \times 10^6/\mu L$ which was maintained till next donation interval, while serum ferritin showed mean increase of 18.9 ng/ml from baseline (visit 1) to 2ndvisit which then decreased significantly at next donation interval (visit 3). Thus all haematological parameters shows an increasing trend from baseline to 2nd visit which was maintained till next donation interval except the serum ferritin which showed a significant decrease ($p < 0.05$; paired t-test and Wilcoxon signed ranks test).

In the placebo group Hb decreased from 13.3 to 12.8 gm/dl i.e. mean decrease of 0.5 gm/dl ($p < 0.05$; paired *t* test), which remained nearly constant at the next donation interval. Hematocrit shows decrease of 1.4 % but maintained at the next visit. RBC count had declined from $4.6\times 10^6/\mu L$ to $4.4 \times 10^6/\mu L$ which was maintained till next donation interval, while serum ferritin showed statistically significant ($p < 0.005$, Wilcoxon signed ranks test) decrease of 17.1 ng/ml from baseline to 2nd visit which remains stable at next donation interval. Thus all haematological parameters shows a decreasing trend from baseline to 2nd visit which was maintained till next donation interval (visit 3).

Considering the iron stores, number of donors with depleted serum ferritin in Iron group decreased from 35 (35 %) to 8 (11.1 %) ($p < 0.05$, Wilcoxon signed ranks test) after iron supplementation but again increased to 21

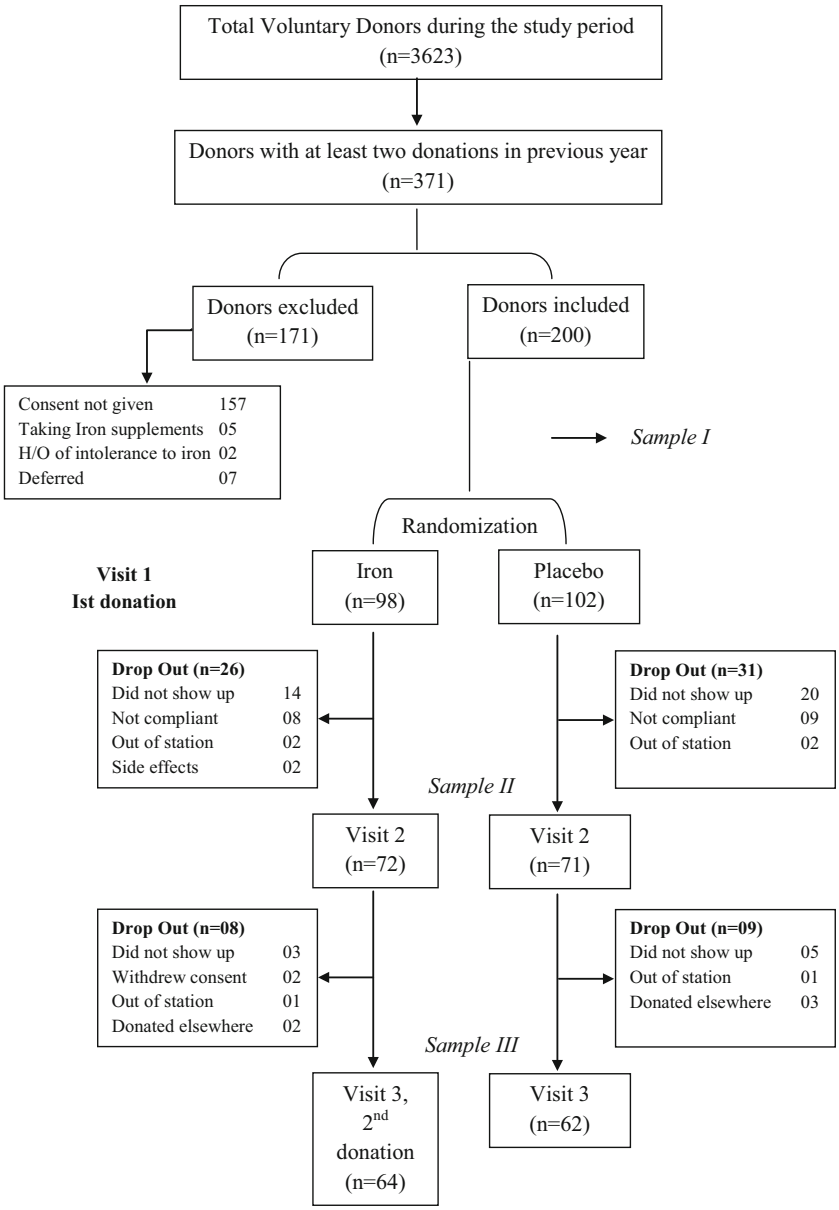

Fig. 2 Flow diagram depicting selection and follow up of donors during the study

(32.8 %) ($p < 0.05$, Wilcoxon signed ranks test) at next donation interval (visit 3). In the Placebo group, donors with depleted serum ferritin increased from 26 (25 %) to 28 (39.4 %) ($p < 0.05$, Wilcoxon signed ranks test) at 1 month after donation which remain nearly same at next donation interval (23 = 37.1 %).

Compliance and Side Effects

Donors were asked about the compliance and side effects at each visit. Compliance with both the regimens was similar as determined by the return rate at 2nd visit and number of capsules remaining at that time. In Iron group, 22 (30.5 %) donors shows significant ($p < 0.05$, Chi square test) adverse effects while in Placebo group 6 (8.5 %) donors had reported side effects. A total of 9 (12.5 %) donors from iron group reported nausea while 6 (8.3 %) donors complained of heart burn sensation after taking iron supplementation. Out of these 2 donors dropped out from study due to side effects of iron supplementation (both had complained of constipation). In Placebo group 3 (4.2 %) and 2 (2.8 %) complained of abdominal cramps and heart burn respectively.

Discussion

Safe and adequate blood supply depends on healthy volunteer blood donors. Prospective blood donors must feel healthy and well on the day of donation and blood centres

Table 1 Iron and Placebo group: demographic profile, donation history and haematological profile

Parameters	Iron (n = 98) Mean ± SD (range)	Placebo (n = 102) Mean ± SD (range)
Demographic details		
Gender	90 (91.8 %)	101 (99 %)
Male	90 (91.8 %)	101 (99 %)
Female	8 (8.2 %)	1 (1 %)
Age (years)	39.8 ± 10.4 (20–58)	38.8 ± 9.5 (20–59)
Wt (kg)	76.7 ± 10.4 (53–100)	77.8 ± 12.3 (50–120)
Dietary habits		
Vegetarian	46 (46.9 %)	47 (46.1 %)
Non vegetarian	52 (53.1 %)	55 (53.9 %)
Donation history		
Age (years) at 1st donation	23.6 ± 5.5 (18–40)	25.6 ± 7.3(18–45)
Total no. of previous donation	30.8 ± 29 (3–118)*	21.1 ± 21.4 (4–104)**
No. of donations in last 12 months	2.6 ± 0.7 (2–4)	2.4 ± 0.6 (2–4)
Interval between last 2 donations (months)	4.5 ± 1.3 (3–8)	4.7 ± 1.3 (3–8)
Haematological parameters		
Hb (g/dl)	12.9 ± 1.3 (10.8–16.1)	13.3 ± 1.2 (10.9–16.4)
Hct (%)	39.9 ± 3.8 (32.9–51.2)*	41.1 ± 3.7 (29.6–48.3)**
MCV (fl)	87.4 ± 6.8 (69.5–105.3)	88.8 ± 7.6 (63.9–103.3)
MCH (pg)	27.9 ± 2.7 (21.7–33.9)	28.8 ± 3.0(20.1–38.7)
MCHC (g/dl)	31.9 ± 1.6 (26.0–35.0)	32.1 ± 1.5(3.3–6.6)
RBC Count (10^{6}/μL)	4.6 ± 0.5 (3.5–6.6)	4.6 ± 0.5 (3.3–6.6)
RDW (fl)	43.7 ± 5.5 (32–55)	44.2 ± 5.1 (34–59)
Serum Ferritin (ng/ml)	43.0 ± 51.8 (0.23–252.2)	47.0 ± 45.6 (0.54–230.1)

* Vs ** p value < 0.05 (Independent sample' *t*' test)

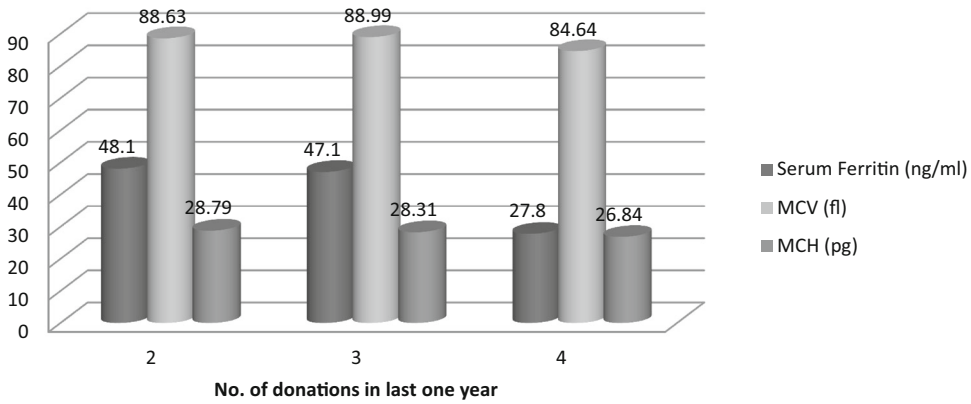

Fig. 3 Serum ferritin, MCV and MCH levels in relation to annual donation frequency (p value < 0.05)

should take additional measures to evaluate the donor's suitability. The selection process attempts not only to ensure that the donor is safe for transfusion to patient but also to protect the donors from undue harm. Blood donation is known to be associated with iron depletion or deficiency particularly in repeat blood donors [4]. In order to explore the usefulness of oral iron supplementation in these regular VBD this randomised controlled trial was conducted.

Most of the donors in our study were males (191 = 95.5 %) while females comprised only a small number 9 (4.5 %). In North Indian study by Makroo and coworkers [6] and another Indian study by Menna et al. [5] female donors contribute only 5.8 and 2.1 % donations respectively. Also going by the statistics collected by the World Health Organisation in June 2011, out of the total number of donations in India only 6 % were contributed by women [6]. This low contribution of female donors may be

Table 2 Evaluation of laboratory parameters at visits 1, 2 and 3

Parameters	Iron group			Placebo group		
	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3
Hb (g/dl)	12.9 ± 1.3 (10.8–16.1)	13.8 ± 1.4* (11.2–16.5)	13.7 ± 1.0# (11.7–16.1)	13.3 ± 1.2 (10.9–16.4)	12.8 ± 0.9* (11.1–15.4)	12.8 ± 0.8# (11–14.8)
Hct (%)	39.6 ± 3.6 (32.9–51.2)	42.8 ± 2.8* (35.4–48.9)	42.9 ± 2.7# (36–49)	41.0 ± 3.8 (29.6–48.3)	39.6 ± 3.1* (32.2–47.4)	39.9 ± 2.9# (34–47)
MCV (fl)	86.7 ± 6.8 (69.5–105.3)	87.2 ± 5.9 (69.1–103.2)	87.1 ± 5.2 (69.9–99.1)	88.5 ± 6.9 (63.9–103.3)	88.1 ± 7.5 (63.5–112)	87.4 ± 7.3 (63.8–101.6)
MCH (pg)	27.8 ± 2.7 (21.7–33.9)	28.0 ± 2.3 (21.4–33.9)	27.8 ± 2.6 (21.6–38.8)	28.6 ± 2.5 (20.1–38.7)	28.2 ± 3.0 (24.1–43.9)	27.6 ± 2.3# (23.6–32.2)
MCHC (g/dl)	32.0 ± 1.7 (26–35)	32.0 ± 1.4 (29.9–35.4)	31.9 ± 1.4 (29.1–35.9)	32.0 ± 1.4 (28.7–35.6)	31.8 ± 1.6 (28.5–39.3)	31.5 ± 1.4# (27.9–34.6)
RBC Count (10^{6}/μL)	4.6 ± 0.5 (3.5–6.6)	5.0 ± 0.5* (4.01–6.59)	5.0 ± 0.5# (4.0–6.2)	4.6 ± 5.2 (3.3–6.6)	4.4 ± 6.2* (3.3–7.1)	4.5 ± 0.6# (3.4–7.2)
RDW (fl)	44.1 ± 5.2 (32–55)	44.3 ± 6.5 (35–67)	43.2 ± 5.6# (33–68)	43.6 ± 4.1 (34–59)	44.5 ± 5.2 (34–54)	43.9 ± 5.5 (34–57.2)
Serum Ferritin (ng/ml)	44.2 ± 56.8 (0.238–252)	63.1 ± 58.3* (0.266–265)	39.5 ± 39.2** (1.59–170)	44.4 ± 40.0 (0.549–230)	27.3 ± 1.9* (0.026–202)	26.4 ± 26.1# (0.654–167)
Iron deficient (%)	35 (35.7 %)	8 (11.1 %)*	21 (32.8 %)**	26 (25.5 %)	28 (39.4 %)*	23 (37.1 %)

* p value < 0.05 compared to sample I (significant change between sample I to II)

** p value < 0.05 compared to sample II (significant change between sample II to III)

p value < 0.05 compared to sample I (significant change between sample I to III)

because of factors like low education status, less awareness and minimal socioeconomic independence in these females. It might also be due to high deferral rates (34.2 %) in women blood donors as compared to men (1.2 %) because of anaemia as observed by Bahadur et al. [7] in northern India. Another reason may be due to bad experience at last donation which leads to decrease in donor return rate and increase in the lapsed donor rate. Bad experience may be because of adverse donor reactions such as hematoma, painful arm and vasovagal reactions which are more common in female donors [8]. At the beginning of the study, all the 200 donors were chosen and divided randomly without any bias and accepted for blood donation after screening procedures. Out of total 57 (28.5 %) of donors had Hb <12.5 gm/dl detected by hematology analyzer on venipuncture sample. Similar results were also observed in other studies [9–11]. Variation observed in the study by Magsudhlu et al. [11] was 7.7 %. This acceptance for donation of donors with low Hb concentration may be a result of sampling error due to hemoconcentration associated with finger puncture method used for screening purposes. Mean serum ferritin of donors enrolled in the study was 45 ± 48.7 ng/ml (Mean ± SD). A total of 61 (30.5 %) donors were found to be iron- depleted (serum ferritin <15 ng/ml) in our study while higher percentage (41 %) of iron deficiency was reported by other investigators [9]. In the present study mean serum ferritin level, MCV and MCH dropped significantly ($p < 0.05$) in relation to annual donation frequency. The similar results were also observed by Mittal et al. [4] as significant mean decrease ($p < 0.001$) in serum ferritin after three blood donations per year, the values being 21.36 versus 55.5 ng/ml in those donors who came for the first time. Similar results were also observed by other investigators [9, 12] The reason for iron deficiency in donors with repeated donations is that the iron demand increases with number of annual blood donation which cannot be compensated by iron absorption and results in an iron deficiency [13]. The prevalence of iron deficiency is related to frequency of blood donation rather than to cumulative total of donations [4, 13]. There was also no significant influence of total number of previous lifetime donations on the serum ferritin levels in the present study though mean serum ferritin (26.9 ng/ml) was lower in donors who had donated more than 75 times compared to others but the difference was not statistically significant. These findings show that there is definite need for iron supplementation programs in regular blood donors.

In this study total of 200 donors were randomly divided into two group Iron and Placebo group. Of the 200 donors, 74 (37 %) donors dropped out, yielding a dropout rate of 35 % in Iron group and 39 % in the Placebo group. Similar drop-out rates (38.5 %) were reported by Maghsudlu et al. [12] while higher percentage (47.5 %) of dropout was reported by other study [14]. In the study by Rosvik et al. [15] and Waldvogel and others [16] drop out

Table 3 Comparison of studies showing the response in haemoglobin and ferritin

Study	Drug used	Dose (mg)	Duration	Hemoglobin			Ferritin		
				Initial mean Hb (gm/dl)	Mean Hb after iron supplementation (gm/dl)	Net increase (gm/dl)	Initial mean serum ferritin (ng/ml)	Mean serum ferritin after iron supplementation (ng/ml)	Net increase (ng/ml)
Ossorio et al. [12]	Ferrous sulphate	100	O.D for 20 days	M-12.2 F-12.0	M-12.9 F-13.5	M-0.7 F-1.5	ND	ND	ND
Patterson et al. [20]	Ferrous sulphate	105	O.D for 12 weeks	ND	ND	ND	9	24.8	15.8
Pittori et al. [19]	Ferrous sulphate	80	For 120 days	13.1	13.9	0.8	6.9	25.2	18.3
Waldvogel et al. [16]	Ferrous sulphate	80	For 4 weeks	12.6	13.5	0.9	15.3	28	12.8
Present study	Ferrous fumarate	98.6	For 21 days	12.9	13.7	0.8	44.2	63.1	18.1

was 21.3 and 5.8 % which was less than the present study, which might be because of single follow up visit in their study. In the present study iron supplementation was given in the form of ferrous fumarate 300 mg per day containing 98.6 mg elemental iron (single drug among ferrous salts containing 32.87 % elemental iron per 100 mg) to be taken once daily for 21 days. At our centre volume of whole blood collected from the donor depends on donor's weight: 45–60 kg—350 ml and >60 kg—450 ml. For each unit of blood collected (350/450 ml), a donor loses about 175/225 mg of iron. Dose used in our study (2100 mg elemental iron) was set according to iron loss from donation (considering the iron absorption to be around 10 % of oral dose 2000 mg of elemental iron will be needed to replenish 200 mg of iron which is generally lost in one unit of blood donation). This dose was also supported by earlier studies [17, 18].

Donors in the Iron group had a significant ($p < 0.05$) increase in mean Hb from the baseline (12.9 gm/dl) to one month after donation (13.8 gm/dl) Ossorio et al. [12] from Germany showed prompt and maintained recovery of Hb concentrations after iron treatment (12.9 ± 0.3 and 13.8 ± 0.2 gm/dl) in male and female donors with initially low Hb values (12.2 ± 0.6 and 12.0 ± 0.5 gm/dl). Net increase in Hb level of 0.8 gm/dl was observed by Pittori et al. [19] and Waldvogel et al. [16] also observed increase from 12.6 gm/dl to 13.5 gm/dl in iron group (Table 3). Whereas in the Placebo group mean Hb decreased significantly from 13.3 to 12.8 gm/dl. Similar decrease in Hb was observed in other studies [16, 19]. This reflects increase in haematopoiesis in the iron group due to oral iron supplementation. These changes in Hb remain stable over next donation interval. Study by Pittori et al. [19] shows increase in Hb from 13.1 ± 0.4 to 13.6 ± 0.6 gm/dl at 2 months interval (after supplementation of 80 mg ferrous sulphate/day) which increased to 13.9 ± 0.8 gm/dl assessed at next donation interval after 4 months (iron supplementation was continued more for 60 days after 1st follow up) while by Ossorio et al. [12] shows maintained recovery of Hb concentrations in subsequent blood donations.

Donors in Iron group in present study had a significant increase in mean serum ferritin from 44 to 63.1 ng/ml at one month after donation (visit 2) (net increase of 18.1 ng/ml). Study by Pittori et al. [19] shows similar increase in serum ferritin from 6.9 to 19.02 ng/ml while study by Waldvogel and colleagues [16] shows net increase in mean serum ferritin of 12.8 ng/ml and study by Patterson et al. [20] shows net increase in mean serum ferritin of 15.8 ng/ml (Table 3). In the Placebo group mean serum ferritin decreased from 44.4 to 27.3 ng/ml in the present study. Studies by Waldvogel et al. [16] and Rosvik et al. [15] showed similar results. At third visit (at next donation interval) mean serum ferritin significantly decreased from 63.1 to 39.5 ng/ml in the donors who had received iron for three weeks. In the study by Pittori et al. [20] mean serum ferritin levels increased from 19.0 to 25.2 ng/ml at next donation interval due to the fact that they had continued the iron supplementation for 60 more days (total 120 days) after first follow up visit (at 2 months) while in our study we had given the supplementation only for 21 days. The mean Hb however remain higher than baseline at subsequent measurement due to utilisation of iron stores continuously for synthesis of Hb. The results showed that one time oral iron supplementation (2100 mg) was not sufficient to sustain the iron stores over a period of 3 months after the donation of 350 ml whole blood. It indicates that regular oral iron supplementation after each blood donation is required in repeat regular voluntary donors to prevent depletion of iron stores.

Side effects with ferrous salt were significantly ($p < 0.05$) more than those observed with placebo. This significance resulted mainly due to nausea reported by 9 donors and constipation by 4 donors in our iron group. Two donors in our study population dropped out due to severe constipation by iron therapy. Waldvogelet al [16] also observed constipation as a significant side effect of iron supplementation. More-over despite this adverse effects adherence to treatment was more than 90 % and were similar in both groups.

In conclusion, serum ferritin levels decrease significantly in relation to total annual donation frequency. In our study 3 weeks (21 days) of oral iron therapy (98.6 mg elemental iron/day) improved Hb and serum ferritin levels initially, but the increase was not sustained. There is need to evaluate increased dosage and/or duration of iron supplementation, although increase in dose may decrease the compliance. In the absence of oral iron supplementation there is progressive reduction in iron stores. Policy for investigation and treatment of iron deficiency state and anaemia need to be incorporated as a part of voluntary blood donation program. Alternatively it may be included as a component of donor haemovigilance programme.

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