

Comparison of daily vs. weekly single-dose ferrous sulphate treatment in female Junior High School students with iron deficiency anemia

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ABSTRACT

Dedy Afandi, Sri Mulatsih, Madarina Julia - *Comparison of daily vs. weekly single-dose ferrous sulphate treatment in female Junior High School students with iron deficiency anemia*

Background: Compliance of daily treatment of iron deficiency anemia in children is still low. The compliance will be increased if the iron supplementation is given weekly. Previous study showed that there was no significant difference in the increase in hemoglobin level between daily and weekly treatment in prepubertal children.

Objective: To study the difference in the increase in hemoglobin and serum ferritin levels between daily and weekly single-dose treatment of ferrous sulphate in female junior high school students with iron deficiency anemia after menarche.

Methods: This was a quasi-experimental study recruiting 179 and 174 anemic female students in the weekly and daily group, respectively. They receive weekly or daily single-dose of ferrous sulphate capsules. Hemoglobin levels were measured before and after the 12 weeks treatment, while serum ferritin levels were measured before and after in a subset of the study subjects.

Result: Mean \pm SD levels of hemoglobin before and after iron supplementation were 11.18 ± 0.51 and 12.79 ± 0.63 g/dl ($p=0.001$) in the weekly group, and 11.17 ± 0.61 and 12.68 ± 0.57 g/dl ($p=0.001$) in the daily group. Mean \pm SD levels of ferritin before and after iron supplementation were 6.95 ± 1.85 and 41.5 ± 33.93 ng/ml ($p=0.001$) in the weekly group, and 6.61 ± 2.17 and 40.7 ± 22.73 ng/ml ($p=0.001$) in the daily group. The prevalence of anemia after supplementation is similar in both groups, i.e. 6.7% in the weekly group and 8.0% in the daily group ($p=0.63$). There were no significance difference in the occurrence of side effects of diarrhea and nausea in both groups ($p>0.05$).

Conclusion: This study concluded that daily vs. weekly ferrous sulphate supplementation did not result in significantly different level of both hemoglobin and serum ferritin after treatment. The difference in the occurrence of side effects was also not statistically significant.

Key words: anemia - iron deficiency - hemoglobin level - serum ferritin level - ferrous sulphate

ABSTRAK

Dedy Afandi, Sri Mulatsih, Madarina Julia - *Pemberian sulfas ferrosus dosis tunggal harian dibanding mingguan pada siswa dengan anemia gizi besi*

Latar Belakang: Kepatuhan terhadap pengobatan anemia defisiensi besi yang diberikan tiap hari pada anak masih rendah. Kepatuhan akan meningkat bila suplementasi besi diberikan tiap minggu sehingga pengobatan akan berhasil. Hasil penelitian sebelumnya tidak ada perbedaan peningkatan kadar hemoglobin yang bermakna pada dosis tiap hari dan tiap minggu pada anak prapubertas.

Tujuan: Mengetahui ada tidaknya perbedaan peningkatan kadar hemoglobin dan kadar ferritin serum antara pemberian sulfas ferrosus dosis tunggal harian dan dosis tunggal mingguan pada remaja putri SMP pasca-menarche yang mengalami anemia defisiensi besi.

Metode: Penelitian ini berdisain kuasi-eksperimental. Subyek penelitian dikelompokkan menjadi 2 kelompok, 179 siswi anemia pada kelompok mingguan dan 174 siswi pada kelompok harian. Mereka mendapatkan suplementasi kapsul sulfas ferrosus mingguan atau harian. Kadar hemoglobin diperiksa sebelum dan sesudah 12 minggu suplementasi. Kadar feritin serum hanya diperiksa pada sebagian subyek, sebelum dan sesudah suplementasi.

Hasil: Rerata \pm SB kadar hemoglobin sebelum dan setelah suplementasi besi pada kelompok tiap minggu adalah $11,18 \pm 0,51$ dan $12,79 \pm 0,63$ g/dl ($p=0,001$); sedangkan pada kelompok tiap hari adalah $11,17 \pm 0,61$ dan $12,68 \pm 0,57$ g/dl ($p=0,001$). Rerata \pm SB kadar feritin serum sebelum dan sesudah suplementasi pada kelompok mingguan adalah $6,95 \pm 1,85$ dan $41,58 \pm 33,93$ ng/ml ($p=0,001$); sedangkan pada kelompok harian adalah $6,61 \pm 2,17$ dan $40,76 \pm 22,73$ ng/ml ($p=0,001$). Prevalensi anemia setelah suplementasi tidak berbeda bermakna di antara kedua kelompok, 6,7% pada kelompok mingguan dan 8,0% pada kelompok harian. Tidak ada perbedaan bermakna kejadian efek samping mual dan diare pada kedua kelompok ($p>0,05$).

Simpulan: Penelitian ini menyimpulkan bahwa pemberian sulfas ferrosus dosis harian dan dosis mingguan tidak memberikan perbedaan kadar hemoglobin dan feritin serum yang secara statistik bermakna. Perbedaan kejadian efek samping juga tidak bermakna secara statistik.

INTRODUCTION

Iron deficiency anemia is still a health problem in both developing and developed countries. Worldwide, 30% of the population is suffering from iron deficiency anemia. The prevalence of anemia is 37% in schoolchildren, 35% in non-pregnant women, and 18% in males. In developing countries, the prevalence of iron deficiency anemia is higher, that is 51% in 1 to 3 year-old children, 46% in 5 to 12 year-old children, 26% in 15 to 49 year old males, 59% in 15 to 49 year-old pregnant women, and 47% in 15 to 49 year-old non-pregnant females.^{1,2}

Iron deficiency anemia in developing girls may be caused by low iron absorption, inadequate intake of iron because of low bioavailability of food containing iron, or in growing up and menstrual periods. Iron deficiency due to blood loss in menstrual period frequently occurs. The total blood loss during menstruation ranges between 25 to 30 mL per month. It reflects iron loss of 12.5-15 mg per month or 0.4-0.5 mg per day of menstruation. In 1983, WHO reported 230 million of 464 million women in developing countries suffered from iron or folate deficiency anemia, or both.²

There are four important factors affecting the success of oral treatment in iron deficiency anemia. They are dose, frequency, dosage form, and compliance. Compliance to daily treatment of iron deficiency anemia was still low.^{3,4,5,6} Several factors affecting the compliance in taking medications are medical provider, drug, and patient. Drug factors

affecting compliance are level of difficulty in administering the drug, signs of improvement after treatment, the total duration of medication, and the side effects of the drug.^{3,4,5,6}

Iron supplementation in the form of iron tablet has been proven to increase iron status faster, especially in target groups such as schoolchildren, girls, and pregnant women. Iron tablet may cause gastrointestinal complaints which may results in the difficulty in motivating patients to take the tablet daily. Incompliance is one of the cause of treatment failure in iron deficiency anemia.⁷ One of the feasible strategies to solve the operational problem of multivitamin and mineral supplementation is to give in lower doses and less frequency, not daily.^{3,4,5,6}

Daily iron supplementation was better than intermittent supplementation in preventing anemia in pregnant women, but there was no difference in other adults and children.³ Daily iron supplementation increased hemoglobin level better than twice-a-week supplementation.^{4,5,6} Weekly iron supplementation did not result in different language and mathematic ability compared to daily supplementation.⁸ Ferrous sulphate once or three times a day gave no different result in anemia improvement without any side effects with similar total dose.⁹ In this study we are comparing the treatment response of daily vs. weekly ferrous sulphate supplementation in junior high school female students with iron deficiency anemia.

METHODS

This was a quasi-experimental study conducted in MTsN Depok and SMPN Depok, Sleman in 2008. Subjects were classified into 2 groups, one group was given weekly treatment while the other group was given daily treatment of ferrous sulphate tablets. The allocation of subjects into treatment groups were not done randomly. It was determined by the researcher. Anemic female students from SMPN were assigned to daily treatment, while anemic female students from MTsN were assigned to weekly treatment.

Both groups were given treatment for 12 weeks. Group MTsN was given ferrous sulphate capsule 42 mg/kgBW weekly, and group SMPN was given ferrous sulphate capsule 6 mg/kgBW daily. Drugs were given and taken in the School Medical Unit Room in the school and were observed by the School Medical Unit teacher.

The study was started by screening hemoglobin levels of female students in both junior high schools. Screening was conducted on 560 female students in the public junior high school (SMPN) and the religious public junior high school (MTsN). In those found to be anemic, serum ferritin level was measured in sub sample of the subjects. Fifty students from each group were randomly chosen to have their serum ferritin levels measured.

After 12 weeks of supplementation, the hemoglobin and ferritin levels of both groups were again measured. T-test was used to analyze the difference in the mean levels of serum ferritin and hemoglobin between the two treatment groups before and after intervention. Data were analyzed with SPSS program. Hypothetical test decision was based on significancy level of 0.05.

RESULTS

There were 560 female students screened, 285 students in MTsN and 275 students in SMPN. Out of 285 MTsN students there were 187 students who had Hb level <12 g/dL (65.6%), while out of 275 SMPN students there were 186 students who had Hb level <12 g/dL (67.6%). The average prevalence of anemia in both schools was 67.0%.

From 187 MTsN students who had anemia, 8 students were not included in this study: 5 declined

to join, 2 were suffering from asthma and typhoid fever, respectively, and 1 had Hb level of 6.8 g/dL and was referred to the hospital. From 186 SMPN students who had anemia, 13 students were not included in this study: 8 declined to join, 2 were recovering from illnesses, and 2 had Hb level of 7.6 g/dL and were referred to the hospital. This study included 179 female students of MTsN who were given weekly iron supplementation, and 174 female students of SMPN who were given daily iron supplementation.

From 179 MTsN anemic students, 50 students were taken randomly for serum ferritin level measurement. Thirty-one students (62.0%) had serum ferritin level of <12 ng/mL. Similarly, from 174 SMPN anemic students, 50 students were taken randomly for serum ferritin level measurement. It resulted in 32 students (64.0%) had serum ferritin level of <12 ng/mL.

Characteristics of the study subjects were shown in TABLE 1 and 2. There was no significant difference in the average of parental educational level, parental income, the subjects' age, body weight, menstrual cycle, duration of menstruation, menstrual pattern, and hemoglobin level in the two groups at the beginning of the study.

After 12 weeks, the average of hemoglobin and serum ferritin levels between the two groups was not significantly different (TABLE 3 and 4). In each group, iron supplementation resulted in significant increase in hemoglobin and serum ferritin levels (TABLE 5).

The occurrence of side effects of nausea and diarrhea were not significantly different between the two groups (TABLE 6).

After supplementation, the prevalence of students who were still suffering from anemia was not significantly different between the two groups (TABLE 7). From 100 students who had their serum ferritin level measured, 7 students (18.9%) of those who had normal serum ferritin level before iron supplementation were still anemia after supplementation. On the other hand, all students whose serum ferritin level before iron supplementation were low, recovered from anemia after supplementation. The difference was statistically significant (TABLE 8).

TABLE 1. Characteristics of the study subjects

Variables	Weekly dose n = 179	Daily dose n = 174	p
Parental educational level (%)			
SD (elementary school)	40(22.4)	33(19.0)	0.86*
SMP (junior high school)	64(35.8)	62(35.6)	
SMA (senior high school)	72(40.2)	76(43.7)	
PT (university)	3 (1.7)	3(1.7)	
Mean±SD parental income (million Rp)	1.02±0.31	1.03±0.31	0.56**
Mean±SD age (years)	14.07±0.80	13.96±0.83	0.20**
Mean±SD body weight (kg)	37.02±1.98	36.83±1.97	0.37**
Mean±SD menstrual cycle (days)	28.03±0.81	27.98±0.92	0.57**
Mean±SD duration of menstruation (days)	5.67±0.99	5.67±0.97	0.73**
Menstrual pattern (%)			
Regular	171(95.5)	169(97.1)	0.57*
Irregular	8(4.5)	5(2.9)	
Mean±SD initial hemoglobin level (g/dL)	11.18±0.51	11.17±0.61	0.72**

* Pearson Chi Square

** Independent Sample T-test

TABLE 2. Characteristics of the study subjects who had serum ferritin level measurement

Variables	Weekly dose n = 50	Daily dose n = 50	p
Parental educational level (%)			
SD (elementary school)	40(22.4)	33(19.0)	0.86*
SMP (junior high school)	64(35.8)	62(35.6)	
SMA (senior high school)	72(40.2)	76(43.7)	
PT (university)	3 (1.7)	3(1.7)	
Mean±SD parent's income (million Rp)	1.02±0.37	0.96±0.28	0.56**
Mean±SD age (years)	14.0±0.45	14.63±0.79	0.20**
Mean±SD body weight (kgs)	36.90±2.13	36.96±2.0	0.90**
Mean±SD menstrual cycle (days)	28.06±1.06	28.06±0.95	0.99**
Mean±SD duration of menstruation (days)	5.64±0.91	5.81±1.06	0.51**
Menstrual pattern (%)			
Regular	171(95.5)	169(97.1)	0.54*
Irregular	8(4.5)	5(2.8)	
Mean±SD initial serum ferritin level (ng/mL)	16.01±13.62	18.78±20.48	0.43**
Mean±SD initial hemoglobin level (g/dL)	11.22±0.54	11.21±0.39	0.93**
Serum ferritin level (ng/mL)			
Low (<12 ng/mL)	31(62.0)	32(64.0)	0.91*
Normal (≥12 ng/mL)	19(38)	18(36.0)	

* Pearson Chi Square

** Independent Sample T-test

TABLE 3. Hemoglobin (Hb) level before and after iron supplementation

Variables	Weekly dose n = 179	Daily dose n = 174	Mean difference 95%CI	p*
Mean±SD initial Hb level (g/dL)	11.18± 0.51	11.17± 0.61	-0.02(-0.14;0.10)	0.72
Mean±SD final Hb level (g/dL)	12.79± 0.63	12.68± 0.57	-0.11(-0.23;0.02)	0.09
Mean±SD change in Hb level (g/dL)	1.51±0.91	1.60±0.83	-0.09(-0.27 ;0.09)	0.34

* : Independent sample T-test

TABLE 4. Serum ferritin level before and after iron supplementation

Variables	Weekly dose n = 31	Daily dose n = 32	Mean difference 95%CI	p*
Mean±SD initial serum ferritin level (ng/mL)	6.61± 1.84	6.60± 2.17	0.35(-0.67;1.36)	0.50
Mean±SD final serum ferritin level (ng/mL)	41.57± 33.93	40.76± 22.73	0.82(-13.68;15.33)	0.91
Change in serum ferritin level (ng/mL)	34.62±33.39	34.15±22.26	0.48(-13.78;14.73)	0.95

* : Independent sample T-test

TABLE 5. The effect of iron supplementation on hemoglobin (Hb) and serum ferritin level

Variables	Initial level	Final level	Mean difference 95%CI	p*
Hemoglobin (g/dL):				
Weekly dose (Mean±SD)	11.18± 0.51	12.79± 0.63	1.60 (1.48;1.73)	<0.001
Daily dose (Mean±SD)	11.17± 0.61	12.68± 0.57	1.51(1.38;1.65)	<0.001
Ferritin (ng/dL):				
Weekly dose (Mean±SD)	6.95±1.85	41.58±33.93	34.62 (22.38;46.87)	<0.001
Daily dose (Mean±SD)	6.61± 2.17	40.76± 22.73	34.15 (26.12;42.18)	<0.001

* : Paired T-test

TABLE 6. Side effect of iron supplementation in both groups

Variables	Weekly dose	Daily dose	RR 95%CI	p*
Diarrhea	n=138	n=128		0.63
Positive	124 (89.9%)	113 (88.3%)	1.08 (0.73-1.61)	
Negative	14 (10.1%)	15 (11.7%)		
Nausea	n=165	n=159		0.28
Positive	126(76.4%)	113(71.1%)	1.15 (0.89-1.49)	
Negatif	39 (23.6%)	46 (28.9%)		

* : Pearson Chi Square

TABLE 7. The prevalence of students still suffering from anemia after iron supplementation

Group	Anemia n(%)	Not anemia n(%)	RR 95% CI	<i>p</i> *
Weekly (n=179)	12(6.7)	167(93.3)	0.83 (0.40-1.75)	0.63
Daily (n=174)	14(8.0)	160(92.0)		

* *Pearson Chi Square*

TABLE 8. The prevalence of students still suffering from anemia after iron supplementation based on serum ferritin level before supplementation

Serum ferritin level before supplementation	Anemia n(%)	Not anemia n(%)	RR 95% CI	<i>p</i> *
Normal (n=37)	(18.9%)	30(81.1%)	1.23 (1.06-1.44)	0.001
Low (n=63)	0(0%)	63(100%)		

* *Fisher's exact test*

DISCUSSION

Since more than 90% of anemia in children in the developing countries is caused by iron deficiency, measurement of hemoglobin level, which is cheap and can be easily done, is often used for screening of iron deficiency.² Although serum ferritin level is a better diagnostic test for iron deficiency anemia, it is very seldom used for screening because of its relatively expensive cost.^{1,2,7}

In practice, response to treatment may help establishing iron deficiency anemia. A 1-2 g increase in hemoglobin level after 3 to 4 weeks treatment with 3-6 mg elemental iron/kg/day is accepted as evidence of iron deficiency. After that, iron supplementation should be continued for another 2 to 3 months.¹⁰

Iron preparation can given either orally or parenterally, oral ferrous sulphate treatment is easier and cheaper, and it gives satisfactory result. Side effects of oral iron medication are nausea, stomachache, and diarrhea.⁴

Twice-a-week iron supplementation with supervision is significantly better than daily iron supplementation without supervision, especially in term of increase in hemoglobin level.⁴ Daily and weekly single-dose ferrous sulphate resulted in no difference in the increase of hemoglobin level.^{5,6}

In this study, hemoglobin was measured before and after supplementation while serum ferritin was measured before and after only in a subset of the study subjects. There was significant increase in hemoglobin and serum ferritin level in both groups after 12 weeks of iron supplementation. Virtually all anemic students recovered, only 7.4% (26 students) remained anemic. The reason for this non-responsiveness might be because these students were not suffering from iron deficiency anemia. Seven out of 37 students with normal serum ferritin before treatment remained anemia, compared to none out of 63 students with low serum ferritin.¹¹

Iron in this study was given in the form of capsule, for easier administration. Side effect of nausea was found in the beginning of the study in 39 students in weekly group (11.0%), and 46 students in the daily group (13.0%). Side effect of diarrhea was found in 14 students (4.0%) in the weekly group, and 15 students (4.2%) in the daily group. There was no significant difference between the two groups.

In this study, there were no significance difference in the increase of hemoglobin and serum ferritin level between the weekly and the daily iron supplementation groups. Similar result is reported by Hapsari in Semarang.¹²

CONCLUSION

This study concluded that daily vs. weekly ferrous sulphate supplementation did not result in significantly different level of both hemoglobin and serum ferritin after treatment. The difference in the occurrence of side effects was also not statistically significant.

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