

Review article

Hemoglobin and serum ferritin levels in women using copper-releasing or levonorgestrel-releasing intrauterine devices: a systematic review

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Received 23 August 2011; revised 3 September 2012; accepted 21 September 2012

Abstract

Background: The use of intrauterine devices as a contraceptive method has been steadily growing in developing countries. Anemia in reproductive-age women is a growing concern in those settings.

Study Design: A systematic review of studies with measured hemoglobin and serum ferritin at baseline and after 1 year of use of copper intrauterine devices (IUDs) or a levonorgestrel-releasing intrauterine system (LNG IUS) was performed.

Results: Fourteen studies involving copper IUDs in nonanemic women and 4 studies in anemic women and 6 involving the LNG IUS met the criteria for the systematic review. Meta-analyses for hemoglobin changes showed significant decreases for users of copper IUDs and an increase for the LNG IUS, but with limited data. In general, ferritin levels followed the same pattern.

Conclusion: Decreases in hemoglobin mean values in copper IUD users were not sufficient to induce anemia in previously nonanemic women. Women who are borderline anemic would likely benefit from using the LNG IUS.

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Keywords: Hemoglobin; Serum ferritin; Copper IUD; Levonorgestrel IUD; Anemia

1. Introduction

The World Health Organization estimates that 42% of women in nonindustrialized countries and around 20% of women in industrialized countries are anemic [1]. A blood hemoglobin level of 120 g/L and a serum ferritin level of 15 ng/mL are considered the cutoffs below which a nonpregnant woman is determined to be anemic [2]. Despite the fact that the normal level of serum ferritin, 250 ng/mL, does not itself represent an appreciable amount of iron, the serum ferritin level is considered to be a faithful reflection of body iron stores and, together with hemoglobin, is used to assess a person's iron status. The daily iron requirement for an adult woman of reproductive age is around 2.0 mg.

In developing countries, menstruation has been posited to be a risk factor for anemia. This risk can be exacerbated

when women suffer from other vaginal bleeding disorders, have poor nutritional status and are affected by parasite infections [3–5].

Monthly blood loss at menstruation can be affected by the use of intrauterine devices (IUDs). The main side effect of using a copper IUD is increased or prolonged vaginal bleeding [6]. The late 1980s saw the development of the levonorgestrel-releasing intrauterine system (LNG IUS) called Mirena[®], which releases daily 20 mcg of the hormone directly into the uterus for between 5 and 7 years [7–9]. As well as having excellent contraceptive efficacy [10,11], the device also has a number of therapeutic effects. The reduction of menstrual blood loss has been the subject of numerous reviews [12–15].

The LNG IUS has been determined to be an effective treatment for menorrhagia [16] and a good alternative to hysterectomy in premenopausal women [17]. The reduction in the volume of monthly blood loss (MBL) resulting from insertion of the LNG IUS should result in an increase in iron levels in the body and reduce the prevalence of anemia among this group of women. A systematic review of controlled trials and case series showed that MBL decreased by between 75% and 98% [18]. For severely anemic women,

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it would appear that this treatment alone would probably not be sufficient to prevent anemia, a conclusion also reached by Sivin [15].

The belief that normal menstruation is a risk factor for iron-deficient anemia has recently been challenged in a study that concluded that endometrial thickness is dependent on energy levels, which themselves are correlated to iron levels [19]. A thicker endometrium should thus result in a woman having higher iron levels, and normal menstruation should not affect iron levels and should not be a risk factor for anemia. However, this study was conducted with normal, nonanemic women, and so the findings cannot be extrapolated to a population of anemic women.

If hemoglobin and ferritin levels are increased in menorrhagic women using the LNG IUS, then it is reasonable to assume that there could also be increases in women who menstruate normally. Simultaneously, do levels of these chemicals decrease in women using copper IUDs, which are known to increase MBL, in the course of the first year of use? Copper IUDs are used extensively in countries in the Middle East and Asia, regions that are also known to have high proportions of women who are anemic or iron deficient and potentially have poor health. If copper IUDs decrease iron stores to levels associated with anemia, these women might benefit from use of an LNG IUS, which might increase levels of hemoglobin and ferritin.

This review attempts to answer two fundamental issues to consider when using a copper IUD or the LNG IUS:

1. In normally menstruating women, does use of a copper IUD decrease hemoglobin and ferritin levels? If so, would decreases be sufficient to induce anemia in previously nonanemic woman?
2. In normally menstruating nonanemic women, does use of the LNG IUS increase hemoglobin and ferritin levels?

2. Methods

2.1. Literature search

MEDLINE (via PubMed), Embase, NHS Centre for Reviews and Dissemination (DARE), The Cochrane Library and Popline® were searched for relevant studies. Reference lists in journal articles were also searched. No time limits or language restrictions were enforced. Medical subject headings (MeSH) used included *intrauterine devices copper*, *intrauterine devices medicated*, *levonorgestrel*, *progesterone*, *progestins*, *menorrhagia* and *anemia*. The term “*iron OR ferritin OR hemoglobin OR hemoglobin OR hematocrit OR haematocrit*” was also used as a search term in combinations with the MeSH search terms.

2.2. Selection

Criteria for initial review of the reference articles were that hemoglobin or ferritin levels were measured (blood or serum) in participating women at some point during the

study. Studies were excluded if they did not contain information on levels of hemoglobin or ferritin in the blood or serum. In the second review, the following inclusion criteria for women were applied:

- normally menstruating at the start of the study (no studies involving menorrhagic women) and between the ages of 18 and 46 years
- mean normal hemoglobin levels at the start of the study (≥ 120 g/L) or, if the study was specifically conducted in anemic women, not have a mean level ≤ 90 g/L
- mean values of hemoglobin and/or ferritin measured at baseline and at 12 months or a value for the mean difference between these two time periods
- use of the following copper IUDs: TCu 200, TCu 220C, TCu 380Ag (also known as TCu 380A), Nova-T 380, Multiload 250 (ML250) and Multiload 375 (ML375), and Fincoid
- The LNG IUS limited to the Mirena® LNG IUS releasing 20 mcg/day of LNG

Studies including multiple types of IUDs were included, and the review was conducted under the assumption that the presence of any amount of copper and not the surface area of copper on the IUD influences the changes in MBL and consequently the levels of hemoglobin or ferritin. Included in this review are randomized and nonrandomized studies with either open or single-blinded subjects. However, meta-analysis was conducted using the randomized studies.

The primary outcome measure was hemoglobin, and the secondary outcome was serum ferritin levels.

2.3. Data extraction

The review was carried out in accordance with the recommendations of the QUOROM statement [20]. A checklist was used to extract data and included information for study design, inclusion criteria, size, duration, loss to follow-up, termination of treatment and outcome results. When possible, study authors were contacted for clarifications and request for more complete information. Two reviewers carried out data extraction and compiled data. All studies were assessed for methodological quality in the following areas: method of randomization (if applicable), reporting of exclusion criteria of patient groups, number and detail determination of loss to follow-up, blinding (if applicable), and description and reporting of statistical methods used in the analysis.

2.4. Data analysis

Stata version 10 (manufactured in College Station, TX, USA, by StataCorp LP) was used for the statistical analysis [21]. Fixed effects and random effects models were used to calculate and compare pooled results. However, we present only results from the random effects models that better account for heterogeneity observed during the analysis. Due to continuous primary outcomes, standardized mean

differences (SMDs) were used. For the purpose of conducting meta-analyses, missing SEs were estimated by using a value provided for another time point (e.g., baseline mean SE for 12 months SE mean) or averaging the other SEs of the other studies. Further explanation of this reasoning is given in the Results section. Sufficient data were extracted to conduct limited meta-analyses for hemoglobin changes in each of the groups, and these are described in the Results section.

3. Results

3.1. Data retrieval

A total of 910 citations resulted from the database searches. Based on initial review criteria, 120 articles were screened for further consideration. Fifty articles that might have or definitely reported levels of iron, hemoglobin, or ferritin and use of IUDs were identified. Excluded studies include the following: three because the type of IUDs used were excluded from this review [22–24]; three because hemoglobin or ferritin levels were not measured [25–27]; three because subject or study information was insufficient or incorrect [28–30]; one because the main study was cross-sectional [31]; seven because the study period was too short [32–34] or too long [35–38]; and five because they were articles documenting later results of studies already described in earlier papers [9,39–42].

Data from 14 studies in which women had normal levels of hemoglobin at baseline ($Hb > 120$ ng/L) [11,43–55] and data from 4 studies in which women were anemic at baseline (typically $Hb \leq 120$ ng/L) [56–59] were included in the review. Six studies involving the LNG IUS met the inclusion criteria [11,47,52,60–62]. Because some studies compared a copper IUD to the LNG IUS, the total number of studies

included was 21. The breakdown of the data retrieval is shown in Fig. 1.

3.2. Assessment of quality of studies

Of the 21 studies included in the review, 9 were randomized, but only 2 gave a detailed description of the allocation procedure, and in only 3 were subjects blinded. Of those three, one compared copper IUDs to LNG IUS [52]. Some studies were designed to run for only 12 months, while others ran for up to 7 years. Reporting of the exclusion criteria for patient groups varied, with some studies giving detailed descriptions regarding selection of subjects and others providing minimal information. Instead of a mean age, a range was sometimes reported, with few studies reporting neither. Relatively few studies measured both hemoglobin and ferritin. In some studies, mean baseline levels and mean at 12-month follow-up levels of hemoglobin or ferritin were reported, along with SEs of the means; these values were used for the meta-analyses. In other studies, only the mean and SE at baseline were reported, while in others, no SEs were reported for either mean at the two time points.

Numbers and details of terminations and loss to follow-up were reported in the majority of studies but were absent in two of the studies conducted in anemic women using copper IUDs. In copper IUD studies, data for 3293 nonanemic women recruited at the start are summarized with an average termination or loss to follow-up of 14% (3 studies out of 13 did not report termination/loss). For anemic women using copper IUDs, data are summarized for 400 women with an average loss of 17% (two studies out of four did not report termination/loss). Data for 3093 women, with an average loss of 23% (two out of six studies did not report termination/loss) are summarized for studies involving the LNG IUS.

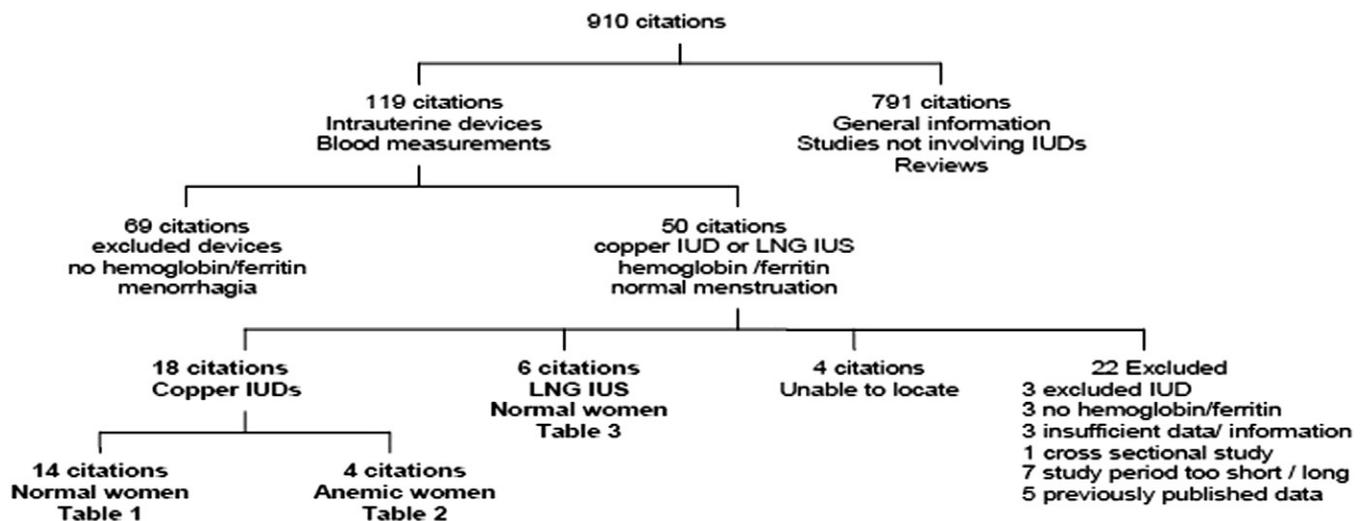


Fig. 1. Data retrieval flowchart.

Reporting of all values of hemoglobin or ferritin at baseline and 12 months and the mean difference together with SEs were rarely provided, with some studies only providing the first two points of data and others the third point. Tests of significance most commonly used were Student's *t* test, Duncan's Multiple Range Test and the Wilcoxon Signed Rank Test. The *p* values for differences in levels between baseline and 12 months were usually reported as $<.05$, $<.01$ or $<.001$ when significant. Detailed characteristics of the studies included in this analysis are presented in [Tables 1, 2 and 3](#).

3.3. Hemoglobin changes: copper IUD use in nonanemic women

Six studies reported significant decreases in hemoglobin levels after 12 months [44,47,50,53,54]. Three of these also reported significant decreases after 6 months. Baseline levels of hemoglobin ranged from 126 to 140 g/L and decreases at 12 months ranged from 3.6 to 9.4 g/L. None of the decreases in the study groups were sufficient to reduce the mean level of hemoglobin to below 120 g/L, the anemia threshold level.

The result of a random-effects model for the five randomized studies included in the meta-analysis is shown in [Fig. 2](#). These randomized studies accounted for 828 of the 2720 subjects included in the review. The overall SMD with a 95% confidence interval (CI) is -0.14 (-0.25 , -0.20), showing that the decrease is modest but significant. The greatest weight is given to the largest study conducted by Andersson et al. [11], and the test for heterogeneity gives a *p* value of .396.

3.4. Ferritin changes: copper IUD use in nonanemic women

All five studies that measured ferritin reported decreases at 12 months compared to baseline, and in three studies, the decrease was significant [43,44,55]. Two of these also reported significant decreases in hemoglobin [44,55], and the other study conducted at two separate sites reported significant decreases in ferritin but not hemoglobin levels after 12 months [43]. Using a regression analysis, the latter study also showed that, at both sites after 12 months, the reduction in serum ferritin was dependent on cumulative MBL, with increasing blood loss resulting in a greater decrease in serum ferritin. Ferritin decreases in the five studies ranged from 5% to 50% and appeared to depend on levels of ferritin at baseline. Women in groups with very low iron stores, reflected by mean ferritin levels <10 ng/mL, reported a slight decrease in mean value, while those in groups with larger iron stores appeared to record a greater decrease in mean value.

3.5. Hemoglobin and ferritin changes: copper IUDs in anemic women

Three studies reported a decrease in hemoglobin, but in only two was the decrease significant at 12 months [56,58]. No studies reported a significant decrease at 6 months. One study actually reported an increase in hemoglobin levels, an

unusual observation, but the baseline mean was extremely low at 107.4 g/L [59]. Termination rates ranged from 0% to 56%, with rates increasing as the number of women in the studies increased.

A meta-analysis of the mean changes in hemoglobin values was conducted for all studies in this group. In the Hassan et al. study [58], standard deviations for hemoglobin values at baseline and 12 months were missing from the report, and we were unable to extract data using statistical methods. For the analysis, an average of the standard deviations of these values in the other three studies was used. This method has the potential to introduce error, but excluding the study from the analysis also runs the risk of introducing bias. In the random-effects model ([Fig. 3](#)), the overall effect estimate is $[-0.29$ (-0.11 , -0.47)]. The overall decrease in hemoglobin at 12 months is not significant with some heterogeneity observed ($p=0.061$).

Decreases in mean ferritin levels were observed for the three studies in which it was measured, but in only one study was the decrease of around 33% significant [57]. In this study, the mean hemoglobin level at baseline was higher than in the other two studies [56,58], which recorded much smaller decreases in ferritin over 12 months.

3.6. Hemoglobin and ferritin changes: LNG IUS use in nonanemic women

Four of the six studies reported a significant increase in hemoglobin after 12 months [47,52,61,62]. Two of the studies reported a significant increase in ferritin, with the mean value doubling after 12 months in one study [63] and increasing by around 40% in the other [60].

Of this group of studies, only three were randomized. However, we could only use two studies for the meta-analysis of hemoglobin changes (data not shown). The study by Sivin ($N=755$) [52] was excluded as no information for baseline or 12-month values of mean hemoglobin were recorded. Even though results show significant increases in hemoglobin [overall effect and 95% CI 0.18 (0.10 – 0.26)], the weight of one of the two studies accounts for more than 90% [11].

4. Discussion

With regards to answering the two questions posed at the start of this review, the findings from the reported studies are somewhat mixed. The meta-analyses show use of a copper IUD by nonanemic women results in a significant decrease in the mean hemoglobin level after 12 months of use. A nonsignificant decrease in hemoglobin is observed for anemic women when using a random-effects model that accounts for heterogeneity. The meta-analysis of hemoglobin changes in LNG IUS users after 12 months reveals a significant increase, but results are based in two studies, one of them with 1821 women.

Table 1
Studies using copper IUDs in normal (nonanemic) women

Study	Randomized	Blinded	Selection criteria	IUD	Size	Mean age (SD)	Termin or loss %	Hemoglobin				Ferritin				
								g/L t=0	g/L t=12	Δ	p [‡] t=12	p [#] t=6	ng/mL t=0	ng/mL t=12	Δ	p [‡] t=12
Andersson et al. (1994) [11]	Y	Not reported	18–38 healthy, ≥1 pregnancy, not breastfeeding or hormonal contraceptives in prior 12 months	Nova T	937	30.3 (4.9)	27	136	-0.9	NS						
Andrade et al. (1988) [43]	Y	Not reported	≥6 weeks since last pregnancy, lactation or use of an oral contraceptive. No use of injectable contraceptives or hormonal medicine	ML 250	14	26.5–28.9 [‡]	29	128	-3	NS	NS	7.1	-0.3	NS	NS	
Andrade et al. (1988) Juiz De Fora, Brazil [43]	N	Not reported	Women aged 25–34, parity 1 or 3, gravida	ML 250	12	29.0–32.2 [‡]	8	133	-6	NS	NS	23.2	-4.9	NS	<.05	<.05
IUD Clinical Research Group (1987) [54]	Y	Not reported	20–39 healthy, regular menses, normal pelvic exam, no OC <1 year. 3 menses since last IUD/abortion/ parturition HB	ML 375	60		25	133	-2	NS	NS	19.3	-6	<.01	<.05	
Gao et al. (1986) [44]	N	N	Women aged 25–34, parity 1 or 3, gravida	TCu 200	61		25	135	-3	NS	NS	20.7	-4.5	<.05	<.01	
			20–39 healthy, regular menses, normal pelvic exam, no OC <1 year. 3 menses since last IUD/abortion/ parturition HB	TCu 200C	69	20–35	3	127	-7.7	<.01	<.001					
			18–45, healthy, parous, <50 days since last pregnancy, no cervical neoplasia,	T Cu 220c	20	NR	15	137	-8	<.01	<.001	23.4	-6.4	<.05	NS	
Haugan et al. (2007) [45]	Y	N	Attending State Maternity Hospital FP clinic and women who delivered at same hospital. Normal pelvic exam and	Nova T-380	470	NR	23	132	2.3	NS	NS					
			Biphasic menstrual cycles, an MBL of 45 mL, no uterine pathology;	Gyne T 380S	487	NR	25	132	0.17	NS	NS					
Heikkila et al. (1982) [46]	N	N	18–40 attending FP Clinic, healthy, regular menses, no OC, IUD, iron therapy within 6 months,	Nova T	30 [¶]	NR	0	140	-4.3	NS	NS					
			No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	Nova T	40 [§]	NR	0	144	-3.6	NS	NS					
Imperato et al. (2002) [47]	N	N	18–40 attending FP Clinic, healthy, regular menses, no OC, IUD, iron therapy within 6 months,	Nova T 200	30	40.2	22	129	-7	<.05	.01					
			18–40 attending FP Clinic, healthy, regular menses, no OC, IUD, iron therapy within 6 months,	ML 250	27			128	-2	NS	NS					
			No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	ML 375	25			130	-5	<.05	<.05					
Kivijarvi et al. (1986) [55]	N	N	18–40 attending FP Clinic, healthy, regular menses, no OC, IUD, iron therapy within 6 months,	Nova T	14	29.6	15	136	-5	<.02	<.01	34	-19.3	<.01	<.01	
			No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	ML Cu 375	13			136	-5	<.02	<.01					
			No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	Fincoind	13											
Milsom (1990) [49]	Y	Y (single)	No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	ML Cu 250	16	35.7(5.2)	0	135	-1	NS	NS	18	0	NS	NS	
			No pelvic pathology, regular menses, ≥2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	ML Cu 375	18	37.1(6.8)	0	138	-2	NS	NS	26	-3	NS	NS	

Milsom et al. (1995) [48]	N	N	No pelvic pathology, regular menses, ≥ 2 spontaneous menstrual cycles after use of hormonal or IUD or OC. 6 spontaneous menses after delivery, abortion or cessation of lactation	Gyne T 380S	20	37.1(7.2)	10	131	-1	NS	NS	22	-2	NS	NS
Perdon-Nuevo (1982) [50]	Not reported	Not reported	Women attending a family planning clinic. No pelvic pathology. Not using any method of hormonal contraception or IUD 3 months prior to study	TCu 200	21	NR	NR	132	4.1	NS					
				TCu 200C	30			136	-3.5	NS					
				TCu 380A	28			140	-4.4	<.01					
Piedras (1983) [51]	N	N	Hb \geq 138g/L, transferrin saturation index \geq 16%. No OC or injectable contraceptives for 3–6 months prior to	TCu 220	15 (I)	28.9 (21–30)	0	150	-9.4	.0014	NS	6.2	1.7	NS	NS
					15 (II)		0	151	-3.6	NS	.017	40.2	-18.7	NS	NS
Sivin (1984) [52]	Y	Y (single)	18–38, parous, reg exposed to risk of pregnancy, not pregnant, not breastfeeding, no history of ectopic pregnancy, no pelvic pathology. No CV problems, copper allergy, jaundice, diabetes, mental illness, anemia, pathological galactorrhea or severe hirsutism	Cu 380Ag	754	26 (5.5)	33	126	-3.6	<.05					
Wright (1989) [53]	N	N	IUD group: regularly menstruating, normal diet attending FP clinic.	Cu T200	20	19–35	10	129	-8.5	<.05					

[¥] p value for difference at 12 months compared to baseline; individual means for each group not recorded.

[#] p value for difference at 6 months compared to baseline Group I: ferritin <15 ng/mL. Group II: ferritin >15 ng/mL.

[¶] postmenstrual.

[§] puerperal (6 weeks after lactational amenorrhea).

Table 2
Studies using copper IUDs in anemic women

Study	Randomized	Blinded	Selection criteria	IUD	Size	Mean age	Termin or loss	Hemoglobin		Ferritin		p # f=6
								g/L f=0	g/L Δ f=12	ng/mL f=0	ng/mL Δ f=12	
Cheng et al. (1988) [56]	Not reported	Not reported	Normal menses. No abortions 3 months prior to study, no hormonal OC and Hb >= 110 g/L	TCu 220C	30	NR	13	120	-9	28.3	-9.4	NS
Goh et al. (1983) [57]	Y	Not reported	Healthy, regular menses, no pelvic pathology. Not pregnant, no OC or IUD in previous 2 months. No depot progesterone in previous 6 months	ML 250	101	28 (5.7)	33	118	-1.5	45	-15<	.0005
Hassan et al. (1999) [58]	Not reported	N	18–40, healthy, seeking use of IUD or combined OC to be used >= 1 year. Not pregnant, >= 3 months since last pregnancy, not breast feeding, Hb 9–12 g/dL	Cu T380A	246	30 (6)	56	110	-4.1	48.5	-4.7	NS
Rivera et al. (1983) [59]	Y	Y (single)	Women with anemia (Hb <= 12 g/dL) of nutritional origin, no Hb <= 9 g/dL, no OC or IUD use in last 3 months, no injectable contraceptive in last 6 months, >= 40 days postpartum, no contraindications for given contraceptive method	TCu 220C	23	24.8 (1.2)	0	107	1.9			.58 .7

In studies involving copper IUDs and nonanemic women, none of the significant decreases in hemoglobin was great enough to lower the group mean value to below 120 g/L, the threshold for anemia. However, significant decreases in ferritin were found in some studies, sufficient to lower group mean values to around 15 ng/mL, the anemia threshold level, perhaps suggesting that ferritin is rapidly being used to make hemoglobin and accelerating its depletion. Although there is some belief that a level of ferritin as low as 6 ng/mL does not adversely affect a person's iron status, continuously low levels could ultimately have a detrimental effect on hemoglobin level and overall iron status of a woman.

In anemic women using copper IUDs, three quarters of the women were in groups in which significant decreases in hemoglobin were recorded, although somewhat oddly, only in one study did ferritin levels decrease significantly and not to levels below 15 ng/mL. The group means for ferritin at baseline are surprisingly high in these studies, contrary to what would be expected in women with anemic levels of hemoglobin, and the reason for this is unclear.

Finally, in nonanemic women using the LNG IUS, four of the six studies included report increases in hemoglobin levels from baseline, indicating the benefit of a reduction in MBL that occurs with use of this system. More interestingly, levels of serum ferritin are increased by 40%–90% in the two studies in which measurements were made. These findings are very similar to those reported in studies involving menorrhagic women using the LNG IUS [18].

It would appear that there is little evidence that use of a copper IUD by healthy women with normal levels of hemoglobin would significantly diminish iron status to the level at which they would be considered to be suffering from iron-deficient anemia. There is evidence that use of the LNG IUS by nonanemic women raises iron levels, but no studies in anemic women were included in the review, so whether or not iron levels in this group of women would be raised above anemia threshold levels remains uncertain.

A limitation of this review is the fact that, in some studies, the data analysis and presentation — primarily comparison of group means — might be influencing the observed mixed results. A comparison of group means values of hemoglobin might not be the most appropriate way to examine the effects of IUDs on iron status. The group means do not account for the fact that women with varying iron status at baseline might be differentially affected depending on the type of IUD. A better way to present data would be stratifying hemoglobin levels at baseline. This way, it would be possible to verify if the greatest changes might be experienced by women with baseline hemoglobin levels farthest away from the threshold value of 120 g/L. Another possible way would be to show the percentage of women below the threshold value of 120 g/L. Thus, it would be possible to examine changes in the percentage of women with hemoglobin or ferritin levels lower than anemia levels at the start and at 12 months according to type of IUD used.

Table 3
Studies using LNG IUS in nonanemic women 12 months

Study	Randomized	Blinded	Selection criteria	Study group size	Mean age (S D)	Termin or Loss %	Hemoglobin				Ferritin			
							t=0 g/L	Δ t=12 g/L	p t=12	p t=6	t=0 ng/mL	Δ t=12 ng/mL	p t=12	p t=6
Andersson et al. (1994) [11]	Y	N	18–38 healthy, ≥1 pregnancy, not breastfeeding or hormonal contraceptives in	1821	30.3(4.9)	25	135.7	1.9	NS					
Dubuisson et al. (2002) [60]	N	N	35–45, healthy, ≥1 pregnancy. Contraception (hormone, Cu IUD or Progestasert) used in last 6 months discontinued due to poor compliance, poor	203	39 (3)	20	130.8	3.5	<.001	39.1	44.3	<.001		
Imperato et al. (2002) [47]	N	N	Biphasic menstrual cycle, an MBL 45 mL, no uterine pathology	16	40.2	NR	131	12	<.01					
Ratsula et al. (1988) [63]	N	N	18–38, no ectopic pregnancy history, not breastfeeding or PID in last 12 months, no OC or other hormonal preps for 1 month before study	198	NR	NR	137	2.9	NS	38	15	<.05		
Sivin et al. (1984) [52]	Y	Y (single)	18–38, parous, reg exposed to risk of pregnancy, not pregnant, not breastfeeding, no history of ectopic pregnancy, no pelvic pathology. No CV problems, copper allergy, jaundice, diabetes, mental illness, anemia, pathological galactorrhea or severe	755	26 (5.5)	35	ND	2.6	<.05					
Wang et al. (1990) [62]	Y	N	20–40, healthy, parous, requesting contraception. Not breast feeding, Hb ≥12 mg/dL, no pelvic pathology. No hormones/contraceptive last 6 months	100	29.8 (3.3)	10	130	3	<.05	NS				

Nonetheless, we consider a general discussion of the studies included in the review and the meta-analyses to be important. Changes in levels of hemoglobin and ferritin in women using IUDs are not simply related to the type of IUD used. Other factors such as the levels of hemoglobin and ferritin at baseline, the amount of blood lost at menstruation and nutritional intake also determine the overall changes. For most women with normal levels of hemoglobin and ferritin, use of a copper IUD will not adversely affect their iron status. In women who have borderline anemia levels, use of a copper IUD could be detrimental to their iron status and overall health. These women could potentially reap substantial benefits from use of the LNG IUS.

5. Conclusion

The studies included in this review show that women using copper IUDs suffer a significant decrease in group mean hemoglobin level after 12 months compared to baseline. By comparison, a significant increase in group mean hemoglobin level is observed in women using the LNG IUS. A similar pattern was observed for ferritin levels, which are an accurate measure of iron stores.

Further studies that are specifically designed to look at iron levels in women stratified by baseline levels of and/or by extent of MBL should provide a better indication of the long-term effects of different IUDs or the LNG IUS. Similarly, an analysis based on percentages of women who

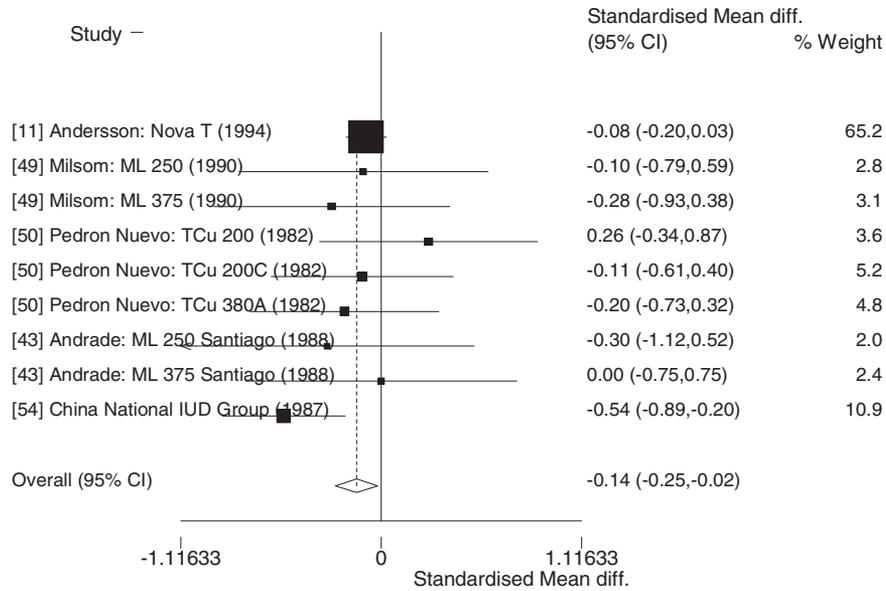


Fig. 2. Random-effects model for hemoglobin change: nonanemic women using copper IUDs.

are anemic at different time points should also provide better answers to these questions.

Given the prevalence of anemia in women in nonindustrialized regions and the concomitant high use of copper IUDs in some of these regions, particularly Asia and the Middle East, it is essential to ensure that women seeking birth control have access to the methods that will be of most benefit to them and least deleterious to their health. Copper IUDs are currently the most widely available, but better-designed studies that might definitively show that use of the LNG IUS by women who are anemic or borderline anemic would considerably improve their iron status, and thus their

overall health, are necessary. If such studies report positive findings, then this form of family planning that has both contraceptive and therapeutic benefits should be promoted and the LNG IUS made available at an affordable price, either through private or public family planning programs.

Acknowledgments

The authors would like to thank Mark Pabst, who helped with the review of studies for inclusion; Paige Passano, who helped with retrieval of articles; Maureen Lahiff, Jack Colford and Nap Hosang, who provided technical and

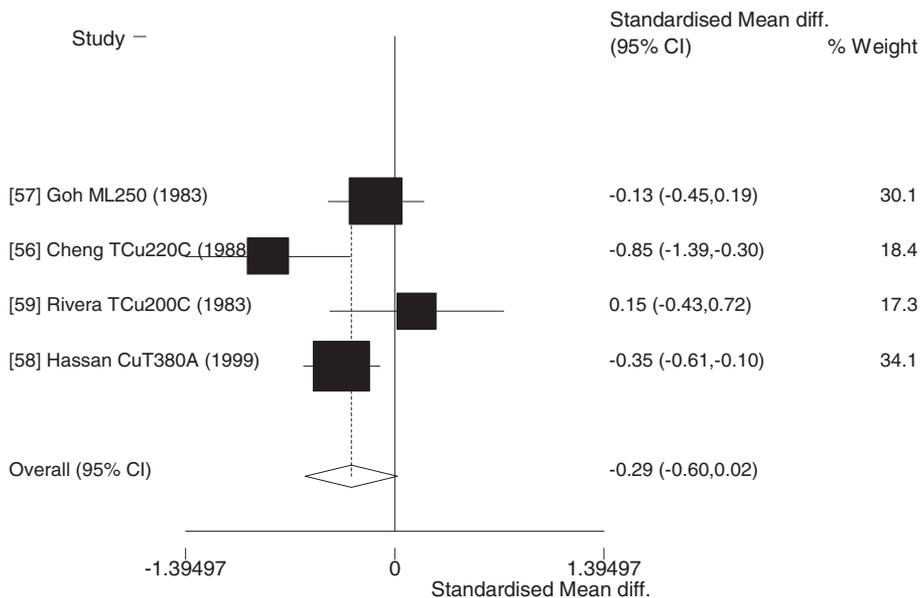


Fig. 3. Random-effects model for hemoglobin changes: anemic women using copper IUDs.

content assistance; and Suzanne Bell, who reviewed and edited the final manuscript.

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