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The effect of vitamin B_1 on bleeding and spotting in women using an intrauterine device: A double-blind randomised controlled trial

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ABSTRACT

Objectives Excessive menstrual bleeding, the most common complication caused by intrauterine devices (IUDs), often leads to discontinuation of use. Our study investigates the effect of vitamin B_1 on menstrual bleeding and spotting after insertion of the TCu380A IUD.

Methods This double-blind, randomised controlled trial involved 110 Iranian women. We recruited women who noted that their menstrual flow (duration, amount, and number of sanitary pads needed) or intermenstrual spotting had increased one month after the insertion of a TCu380A, and randomly assigned them to two groups. The intervention group and the control group received 100 mg of vitamin B_1 or a placebo, respectively, daily, for three months. We followed all participants for four months. The Higham scale was used for estimating the volume of menstrual bleeding. The Mann-Whitney test, paired t-test, independent t-test and Repeated Measure test were used for statistical purposes.

Results In the intervention group the duration of menstrual bleeding, the number of sanitary pads and the amount of spotting decreased significantly compared to the control group ($p < 0.001$).

Conclusion Vitamin B_1 is a safe, natural and cost-effective supplement that is devoid of side effects and reduces menstrual bleeding and spotting caused by a copper bearing-IUD.

KEYWORDS Heavy menstrual bleeding; Intrauterine device; Iran; Spotting; Thiamine; Vitamin B_1

INTRODUCTION

Copper-bearing intrauterine devices (Cu-IUDs) are associated with adverse effects such as dysmenorrhoea and heavy menstrual bleeding that lead to early removal of IUDs in 10% of women[1]. In Iran, 34% of the cases in which the IUD is prematurely discontinued are due to bleeding[2].

For most women who discontinue use of the Cu-IUD within the first year after insertion, the

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primary complaint is heavy menstrual bleeding[3]. Hubacher *et al.* reported that two thirds of 1570 women wearing a Cu-IUD, complained about increased menstrual bleeding in the first nine weeks following insertion and 24% reported intermenstrual spotting[4]. In addition to the inconvenience experienced by women because of bleeding problems associated with IUD use, discontinuation is still a major concern for providers[5].

Several mechanisms have been proposed for the increased bleeding associated with copper IUD use. One major contributing factor is the enhanced fibrinolytic activity in the endometrium induced by copper[6]. An increased production of prostacyclin (PGI_2), that acts as a vasodilator and inhibits platelet aggregation, is another possible mechanism[7]. In Islamic countries, spotting causes many problems for women as, when this happens, they are unable to say their prayers or to engage in sexual activity. A study in Africa, Asia, and Latin America showed that age and religion were significant contributing factors among women who discontinued IUD use after one year[8]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line for the treatment of bleeding due to the IUD: a 2009 Cochrane systematic review of 15 randomised controlled trials showed that treatment with these agents led to a reduction in pain and heavy menstrual bleeding due to IUD use[9]. Yet, there is no general consensus regarding the beneficial effects of NSAIDs. In a large double-blind, randomised controlled trial, 2019 women who were first-time IUD users were instructed to take ibuprofen or a placebo; the intake of 1200 mg of ibuprofen daily during menses (for up to five days each cycle) for the first six months of IUD use did not reduce the incidence of early IUD removal due to heavy menstrual bleeding and pain[10].

The TCu380A is the only IUD that is currently available in public health clinics in Iran, and NSAIDs the sole treatment given for IUD-associated pain and increased menstrual bleeding.

Vitamin B_1

The water-soluble vitamin B_1 (thiamine) plays an essential role in carbohydrate metabolism and neural function. Thiamine deficiency has been associated with anorexia, weight loss, cardiac and neurological signs, and beriberi disease[11]. An early-onset autosomal recessive disorder characterised by megaloblastic anaemia and diabetes mellitus, which responds to the administration of thiamine, has been documented[12].

Little is known about the effect of vitamin B_1 on the vascular system. Thiamine could improve the endothelium-dependent vasodilatation in healthy subjects submitting to an oral glucose tolerance test with ingestion of 75 g glucose[13]. Thornalley *et al.* demonstrated that dyslipidaemia and vascular complications can be prevented in diabetic patients who receive high doses of thiamine supplementation[14]. The author of another study, published in 1996, claimed that vitamin B_1 significantly improved dysmenorrhoea in young girls[15], yet, to the best of our knowledge, this study has not been replicated since and the impressive results reported by the author, after all these years, are still awaiting confirmation. To date, there has been no study on the effectiveness of thiamine on menstrual bleeding and spotting after IUD insertion.

We previously observed that vitamin B_1 intake improved symptoms of dysmenorrhoea and also reduced menstrual bleeding in women not wearing an IUD (unpublished data). We therefore designed a double-blind, randomised controlled trial to investigate the effect of vitamin B_1 on menstrual bleeding and spotting after insertion of the TCu380A IUD.

METHODS

From 2011 to 2013, we recruited 126 women of reproductive age to participate in a double-blind randomised controlled trial. The study was registered with the Iranian Clinical Trials Centre (IRCT:2012073010451N1). Two public health clinics in Borujerd, Iran, were selected for subject recruitment. Borujerd is located in the west of Iran in the Lorestan Province and has a population of 240,654 according to the 2011 census.

The design of the study was approved by the Ethics Committee of Azad University, Borujerd Branch. The inclusion criteria were the following: basic literacy, first time use of the TCu380A IUD, a history of normal menstrual bleeding with duration of 3 to 7 days without spotting, a menstrual cycle lasting 26 to 30 days, use of 10 to 14 sanitary pads per cycle before IUD insertion, and a gravidity ranging between 1 and 4. Women suffering from systemic diseases were excluded from the study.

Those who met the inclusion criteria were scheduled for insertion of the TCu380A, a T-shaped IUD

with 380 mm^2 copper surface that is effective for up to ten years. They were instructed to complete a check-list the first month after IUD insertion and to return for a follow-up clinic appointment. During the follow-up visit, if women claimed that the volume of blood loss and the number of used sanitary pads had increased or mentioned spotting, they were recruited into the study. Participants were assigned in a 1:1 ratio to the use of vitamin B_1 or placebo, in accordance with a random table produced by an Excel programme, with A being assigned to the intervention group and B to the control group. All women signed a written informed consent prior to data collection. Information regarding the duration of the study, the number of follow-up visits, the double-blind nature of the study, as well as details on how to complete the checklists, was provided in the informed consent form.

Intervention

Vitamin B_1 (100 mg) and the placebo were prepared by a person who was unaware of the purpose of the study. Each woman received a packet containing 30 pills (vitamin B_1 or placebo), each month for three months. The placebo, which contained dried starch, had a similar appearance to that of the vitamin B_1-containing pill. Women in the intervention group received 100 mg vitamin B_1 per day during the second, third and fourth months following insertion of the IUD, while those assigned to the control group received the placebo. All participants were followed for one month after completion of the intervention. They were requested to note the amount of menstrual blood lost using the Higham scale[16]. At the end of each month women submitted their checklists and received new packets of vitamin B_1 or placebo. All women were provided a special brand of sanitary pads free of charge for better estimation of blood loss.

Measures

A questionnaire was used to collect participants'socio-demographic data, and a checklist for reporting the bleeding pattern (amount and duration). The volume of blood loss was evaluated by means of the Higham scale, which is a standard scale with a specificity and sensitivity of more than 80%[16]. We assessed the content validity of both the questionnaire and the check list.

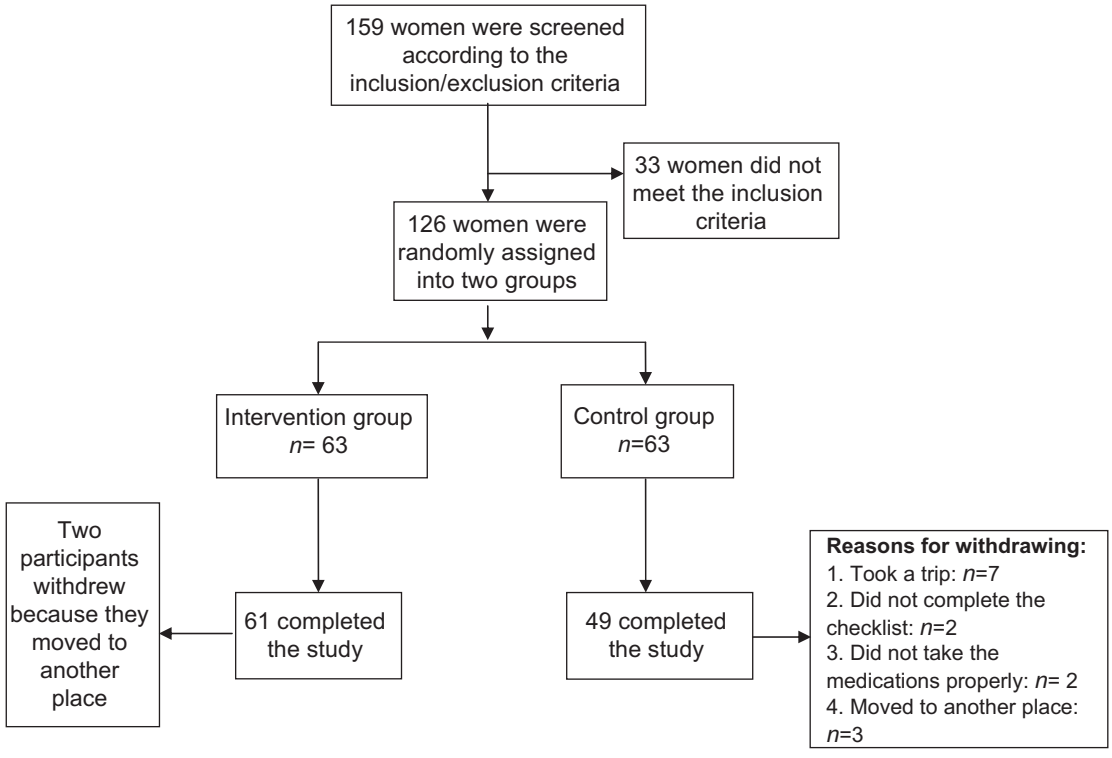

Figure 1 Flow diagram of the recruitment and retention of participants in the study.

Statistics

For data entry and analysis SPSS version 16 was used. Descriptive statistics, the Mann-Whitney test, paired t-test, independent t-test and Repeated Measure (RM) test were used for statistical analysis.

RESULTS

Sixteen women withdrew from the study (14 in the control group and two in the intervention group), and 110 completed the study. The reasons for withdrawing are listed in Figure 1.

There were no significant differences between the two groups in terms of age, age at menarche, length of menstrual cycle, and number of pregnancies ($p > 0.05$) (Table 1).

There was a significant difference between the two groups at five months regarding the length of menstrual bleeding (6 ± 1 vs. 8 ± 1 in the intervention and control groups, respectively; $p < 0.001$) (Figure 2). This difference was significant in the second month and remained so in the third, fourth and fifth months of follow-up ($p < 0.001$). The duration of menstrual bleeding in the intervention group decreased from 8 ± 3 to 6 ± 1 days in the fifth month (Table 2).

The number of sanitary pads used dropped significantly in the intervention group compared to the control group (12 ± 4 vs. 19 ± 4 in the intervention and control groups, respectively; $p < 0.001$). This difference became significant from the second month onwards and remained so until the fifth month of the study inclusive (Table 2).

The two groups differed significantly with regard to spotting after five months of follow-up ($p < 0.001$). Also this difference became significant in the second month and remained significant until the fifth month of follow-up ($p < 0.001$). The percentage of women with spotting decreased from 62% to 17% in the intervention group (Figure 3). There was also a significant difference between the two groups in the duration of spotting (0.4 ± 0.8 vs. 2 ± 2 days in the intervention and control groups, respectively; $p < 0.001$) (Table 2).

One woman in the intervention group and nine in the placebo had their IUD removed by the end of the fifth month. The reasons for early removal in both groups were pain, increased amount of menstrual bleeding, spotting, inability to pray and discontinuation of vitamin B_1 or placebo because of their perceived

Table 1 Socio-demographic characteristics of vitamin B1 and control group.

Variables	*Intervention n = 61 Mean ± SD or n (%)*	*Control n = 49*	*p-value*
Age (years)	28 ± 5	28 ± 4	0.54
Education			
High school	32 (52)	21 (43)	0.62
Secondary high school	26 (43)	24 (49)	
University education	3 (5)	4 (8)	
Job			
Housewife	58 (95)	45 (92)	0.53
Employee	3 (5)	4 (8)	
Mode of last delivery			
Vaginal	53 (87)	38 (78)	0.73
Caesarean section	8 (13)	11 (22)	
Number of pregnancies			
1	10 (16)	11 (22)	0.62
2	27 (44)	24 (49)	
≥3	24 (40)	14 (29)	
Age at menarche	13 ± 1	13 ± 1	0.60
Length of menstrual cycle, days	29 ± 1	29 ± 1	0.85

SD, standard deviation.

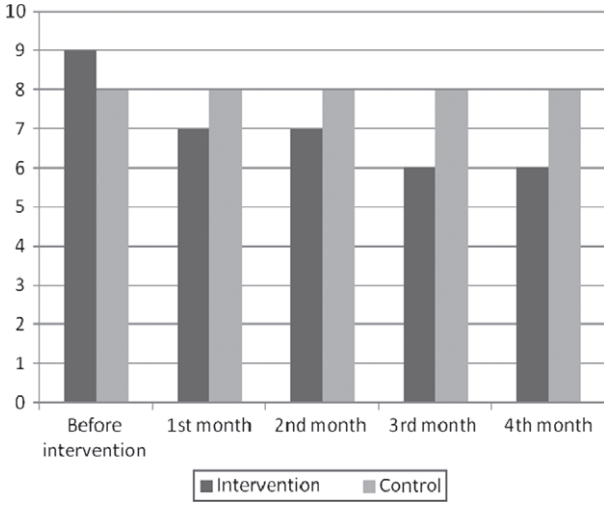

Figure 2 Duration of menstrual bleeding (days) in the two study groups.

ineffectiveness. There were no complaints about side effects related to the treatment in either group.

DISCUSSION

The most common adverse effect of IUD use is increased menstrual bleeding and spotting[1]. The aim of this study was to assess the effectiveness of vitamin B_1 in reducing menstrual bleeding and spotting after insertion of a TCu380A IUD. Usually, women with excessive menstrual bleeding due to an IUD are treated with NSAIDs.

Findings and interpretation

Intake of vitamin B_1 is associated with a significant reduction in the amount of menstrual bleeding and spotting in women who are first-time Cu-IUD users. The number of sanitary pads used was also significantly smaller in the vitamin B_1-treated group compared to the control group. Although we did not directly assess the effectiveness of thiamine on IUD discontinuation, more women in the control group discontinued their IUD use ($n = 9$) than in the intervention group ($n = 1$).

Strengths and limitations of study

To our knowledge, this is the first time that the effect of vitamin B_1 on menstrual bleeding and spotting

Table 2 Duration and severity (number of sanitary pads used) of menstrual bleeding, and spotting: comparison between the intervention and the control group.

	Mean ± SD										
	Before intervention		*1st month of intervention*		*2nd month of intervention*		*3rd month of intervention*		*4th month of intervention*		
Variables	intervention	control	intervention	control	intervention	control	intervention	control	intervention	control	*p-value*
Duration of bleeding (days)*	9 ± 3	8 ± 3	7 ± 2	8 ± 2	7 ± 2	8 ± 1	6 ± 2	8 ± 2	6 ± 1	8 ± 1	< 0.001
Number of sanitary pads*	21 ± 7	21 ± 5	16 ± 4	21 ± 4	13 ± 3	20 ± 4	13 ± 5	19 ± 4	12 ± 4	19 ± 4	< 0.001
Number of days with spotting*	2 ± 2	3 ± 3	0.6 ± 2	2 ± 2	0.5 ± 0.1	2 ± 2	0.5 ± 0.8	2 ± 2	0.4 ± 0.8	2 ± 1	< 0.001
Spotting *n* (%)*	38 (62)	33 (67)	19 (31)	29 (59)	12 (20)	23 (47)	11 (18)	24 (49)	10 (17)	23 (47)	< 0.001

SD, standard deviation.
*p-value is due to the RM test and shows the differences between two groups during five months.

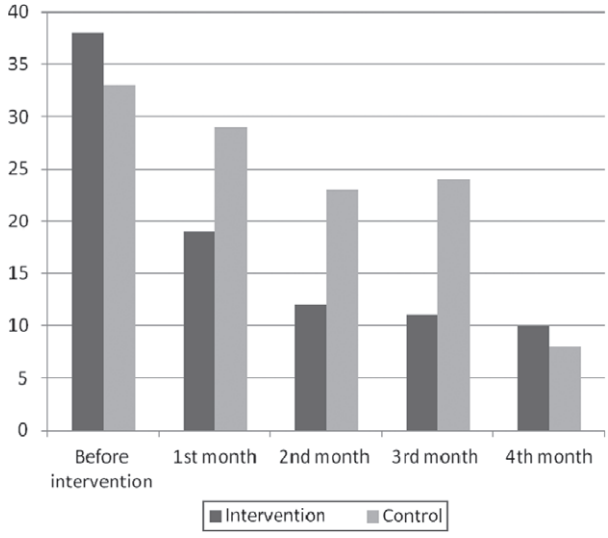

Figure 3 The number of women with spotting in the two study groups.

after IUD insertion has been assessed. Our study was a double-blind, randomised controlled trial with five months of intensive follow-up. Our results demonstrate that the positive effects of vitamin B_1 on bleeding and spotting are evident as early as one month after the intervention. Further, these beneficial effects were sustained after vitamin B_1 was discontinued.

We did not check the micronutrient status of the women before starting the intervention. Perhaps, if this would have been done, we could have identified women with vitamin B_1 deficiency and taken appropriate targeted action.

Differences in the results and conclusions in relation to other studies

Although we have not traced similar studies, a large randomised controlled trial has previously demonstrated the curative effect of vitamin B_1 on dysmenorrhoea[15]. In unpublished research (Master's thesis data), we did assess the effect of thiamine on dysmenorrhoea in young girls and noted a concomitant reduction in menstrual bleeding after three months.

In reaction to the IUD as a foreign body, there is an increased presence of polymorphonuclear leucocytes and macrophages in the endometrium and the endometrial cavity[7,17,18]. This reaction is greater with Cu-IUDs compared to inert ones[19]. Interstitial haemorrhage that causes metrorrhagia with an IUD *in situ* is induced by increased vascularity, congestion, increased vascular permeability, and degeneration with defect formation[20]. IUDs may block, delay or alter in some way the degree of the haemostatic response of the endometrial vessels[17]. Thiamine deficiency is associated with an increased blood flow through the vessels[21]. In addition, even if these observations may not be fully relevant to the context of our study, administration of thiamine has been shown to improve endothelial function in subjects with impaired glucose tolerance, type 2 diabetes and healthy subjects during a phase of induced hyperglycaemia[13,22].

Relevance of the findings: Implications for clinicians

Our study demonstrates that vitamin B_1 supplementation can significantly reduce the amount of menstrual blood loss in women wearing a TCu380A and that it may potentially decrease discontinuation of IUD use because of bleeding. In addition, compared to NSAIDs, thiamine has few side effects.

Unanswered questions and future research

The mechanism whereby vitamin B_1 reduces bleeding is unknown. Further studies should investigate its effects on blood vessels and other factors involved in haemostasis. The beneficial effects on menstrual blood loss we observed in women fitted with a Cu-IUD may also extend to others with heavy menstrual bleeding unrelated to the presence of such a device, and this should be investigated.

Thiamine deficiency often occurs in places with high consumption of refined rice and cereals and low intake of animal and dairy products, in breastfed infants from deficient mothers and in cases of chronic alcoholism[23]. Severe deficiency leading to beriberi has been reported in some parts of Africa and Thailand but little is known about the potential effects of marginal vitamin B_1 deficiency globally[24].

In Iran, because rice and cereals are not fortified with thiamine, vitamin B_1 deficiency is likely to be common, though more research is needed along with measurements of blood levels of thiamine to confirm this.

CONCLUSION

Vitamin B_1 is a safe, natural and cost-effective supplement devoid of serious side effects. Its use, to reduce

heavy menstrual bleeding and spotting experienced by women wearing an IUD, should be considered.

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