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Original Research Article

Comparative Effectiveness of the Levonorgestrel-Releasing Intra-Uterine System versus Tranexamic Acid for Heavy Menstrual Bleeding in Perimenopausal Women

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Abstract

Background: Heavy menstrual bleeding (HMB) affects up to 30 % of perimenopausal women and impairs quality of life. Levonorgestrel-releasing intra-uterine system (LNG-IUS) and oral tranexamic acid (TXA) are guideline-endorsed first-line options, but head-to-head evidence in the perimenopausal age-group remains sparse.

Methods: We performed a 12-month, randomised trial at tertiary hospital in which 200 perimenopausal women (45-54 years) with objectively confirmed HMB (Pictorial Blood-Loss Assessment Chart [PBAC] > 150) were allocated 1:1 to LNG-IUS (52 mg,) or TXA (1.5 g orally three-times daily for up to five days per cycle). Primary endpoint was mean change in PBAC score at 12 months. Secondary endpoints were change in haemoglobin, Menorrhagia Impact Questionnaire (MIQ) score, treatment satisfaction, and adverse events. Intention-to-treat analysis used mixed-effects modelling.

Results: Baseline characteristics were comparable. Mean PBAC fell from 300 ± 55 to 60 ± 18 with LNG-IUS and to 160 ± 35 with TXA (mean difference −100 [95 % CI −113 to −87]; $p < 0.001$). Haemoglobin rose by 1.9 ± 0.4 g/dL versus 0.8 ± 0.3 g/dL ($p < 0.001$). MIQ improved by 30 ± 6 versus 15 ± 5 points ($p < 0.001$). Satisfaction was higher with LNG-IUS (88 % vs 62%). Device expulsion occurred in 4 %, while TXA-related dyspepsia and headache occurred in 18 %.

Conclusion: In perimenopausal women with HMB, LNG-IUS achieved significantly greater reductions in menstrual blood loss, anaemia correction and quality-of-life improvement than cyclic TXA, with acceptable safety. LNG-IUS should be considered the preferred first-line medical therapy when fertility is no longer desired.

Keywords: heavy menstrual bleeding; perimenopause; levonorgestrel intra-uterine system; tranexamic acid; randomised trial; PBAC.

Introduction

Up to one-third of perimenopausal women experience heavy menstrual bleeding (HMB) prolonged (> 7 days) or excessive (> 80 mL) cyclic blood loss, including anovulatory cycles, leiomyomas, adenomyosis and changing sex steroid milieu [1].

Iron deficiency anaemia, absence at work and psychological distress are some of the consequences associated with this condition [2]. The levonorgestrel releasing intra uterine system (LNG IUS) and antifibrinolytic agent tranexamic acid (TXA) are the products supported by the international guidelines as pharmacotherapy during the prioritization of pharmacotherapy to surgery [3,4].

Locally delivered LNG IUS provides 20 mcg levonorgestrel daily, causing endometrial atrophy, and decreasing average menstrual blood loss by 80-96 per cent of heterogeneous populations [5]. When RCTs are used in reproductive aged cohorts, they

prove better than combined oral contraceptives, oral progestogens and non-steroidal anti-inflammatory drugs, and they have add-on contraceptive effectiveness [6]. On the other hand, TXA prevents the activation of plasminogen and minimizes blood loss by 40 60 % when using it during menses [7]. It is preferred by women who want a non-hormonal drug, on demand and long term use might be hindered by compliance and gastrointestinal intolerance.

Although there is quite a lot of data among younger women, there is little evidence on direct comparative evidence, specifically in perimenopause. This age group may alter drug interactions due to the effects of physiological oestrogen withdrawal, rates of fibroid development and other comorbid conditions such as high blood pressure or obesity [8]. Some small observational studies purport that LNG IUS remains effective but convincing head to head randomised data are not found. Clinically, it is imperative to fill this gap as a way of informing shared decision making and reducing unnecessary hysterectomy.

We thus evaluated a pragmatic, multicentred randomised trial against LNG IUS compared to cyclic TXA in perimenopausal women with HMB measured objectively. We conjectured that LNG IUS would confer greater menstrual blood loss reduction and quality-of-life benefit after 12 months, and an acceptable tolerance profile than 1600 mg klomifen.

Materials and Methods

Design and setting: A 12 month, prospective, open label, parallel group randomised controlled trial was conducted between March 2023 and April 2025.

Participants: Regular and irregular cycle women 45 54 yrs of age whose HMB (PBAC >150 in at least 2 baseline cycles) was confirmed objectively were studied. Desire to preserve future fertility, Uterine distortion of the cavity making insertion of an IUS impossible, submucosal fibroids > 3cm, Endometrial hyperplasia, Coagulopathies, Current systemic use of progestogens and within three months, contraindications to TXA (e.g. active thrombosis or colour vision defect) or LNG IUS (e.g. known pelvic infection or unexplained bleeding). An informed consent was taken.

Randomisation and masking: Stratified by centre through a computer generated block size of eight, the participants were assigned 1:1 to either LNG IUS or TXA. Randomization was obscured in non-transparent envelopes broken by an independent nurse. Due to different routes, both participants and clinicians were not blinded but outcome assessors and statisticians were blinded.

Interventions: LNG IUS (52mg levonorgestrel and the release of 20mcg/day) was introduced within seven days after the onset of menstruation. TXA group was given 1.5 g tablets thrice daily up to a maximum of five days beginning day 1 of menses throughout 12 menstrual cycles. Coinverse iron treatment was allowed.

Outcomes: Primary outcome: change in mean PBAC score from baseline to 12 months. Secondary outcomes: PBAC change at 3 and 6 months; haemoglobin and ferritin; MIQ score; treatment satisfaction (5 point Likert); adverse events; discontinuation.

Assessments: PBAC diaries were completed for every cycle. Haematologic indices were measured at baseline, 6 and 12 months. MIQ was administered at same time points. Adverse events were recorded at quarterly visits.

Sample size: Assuming a 40 point greater PBAC reduction with LNG IUS (SD 70), $\alpha = 0.05$ and 90 % power, 88 women per arm were required; anticipating 10 % attrition, we enrolled 100 per arm.

Statistical Analysis: Intention to treat population included all randomised participants. Mixed effects linear models assessed treatment, time and interaction, with random intercepts for subjects. Categorical outcomes were compared using χ^2 or Fisher's exact test. Missing data were handled by maximum likelihood estimation. $P < 0.05$ denoted significance. Analyses used Stata 18.

Results

Participant flow and baseline data: of 274 screened women, 200 were randomised (LNG IUS = 100; TXA = 100). Follow up at 12 months was 94 % and 91 %, respectively.

Baseline characteristics were comparable (Table 1). Mean age was 48.9 ± 2.5 years; 38 % had fibroids ≤ 3 cm; mean baseline PBAC 300 ± 55.

Primary outcome At 12 months, mean PBAC decreased by 240 ± 50 points with LNG IUS versus 140 ± 45 with TXA (adjusted mean difference −100 [95 % CI −113 to −87]; $p < 0.001$) (Figure 1). Fifty eight percent of LNG IUS users achieved PBAC < 20 (amenorrhoea) compared with 12 % of TXA users ($p < 0.001$).

Secondary outcomes Haemoglobin rose from 10.8 ± 1.3 to 12.7 ± 1.1 g/dL with LNG IUS and to 11.6 ± 1.2 g/dL with TXA ($p < 0.001$). MIQ improved significantly in both groups, favouring LNG IUS (mean change 30 vs 15 points; $p < 0.001$) (Figure 2).

Treatment satisfaction was "very satisfied/satisfied" in 88 % vs 62 % ($p < 0.001$).

Safety: Adverse events are summarised in Table 4. LNG IUS expulsions (n = 4) and hormonal side effects (acne 6 %, breast tenderness 5 %) were uncommon. No pelvic infections occurred. TXA related dyspepsia (13 %), headache (11 %) and myalgia (4 %) led to discontinuation in eight women. One superficial thrombophlebitis was reported in the TXA arm; no deep vein thromboses or pulmonary emboli occurred.

Table 1: Baseline characteristics (n = 200)

Characteristic	LNG-IUS (n = 100)	TXA (n = 100)	p value
Age, years	48.8 ± 2.4	49.0 ± 2.6	0.62
BMI, kg m^{-2}	29.3 ± 4.5	28.9 ± 4.3	0.48
Nulliparous, %	14	16	0.68
Fibroids ≤ 3 cm, %	39	37	0.77
Baseline PBAC	301 ± 54	299 ± 56	0.79
Haemoglobin, g/dL	10.8 ± 1.3	10.8 ± 1.2	0.97

Table 2: Change in PBAC score

Time-point	LNG-IUS	TXA	Mean diff (95 % CI)	p
3 mo	−180 ± 45	−80 ± 40	−100 (−113 to −87)	< 0.001
6 mo	−225 ± 48	−120 ± 42	−105 (−119 to −91)	< 0.001
12 mo	−240 ± 50	−140 ± 45	−100 (−113 to −87)	< 0.001

Table 3: Quality-of-life and haematologic outcomes (12 mo)

Outcome	LNG-IUS	TXA	p
MIQ change (↓)	30 ± 6	15 ± 5	< 0.001
Haemoglobin ↑ g/dL	1.9 ± 0.4	0.8 ± 0.3	< 0.001
Ferritin ↑ µg/L	24 ± 6	12 ± 5	< 0.001
Satisfaction ≥ 4/5, %	88	62	< 0.001

Table 4: Adverse events and discontinuation

Event	LNG-IUS (n = 100)	TXA (n = 100)	p
Any adverse event	28	34	0.29
Hormonal side-effects	11	—	—
GI discomfort	2	13	< 0.01
Headache	3	11	0.03
Venous events	0	1	0.32
Device expulsion	4	—	—
Discontinued therapy	6	14	0.04

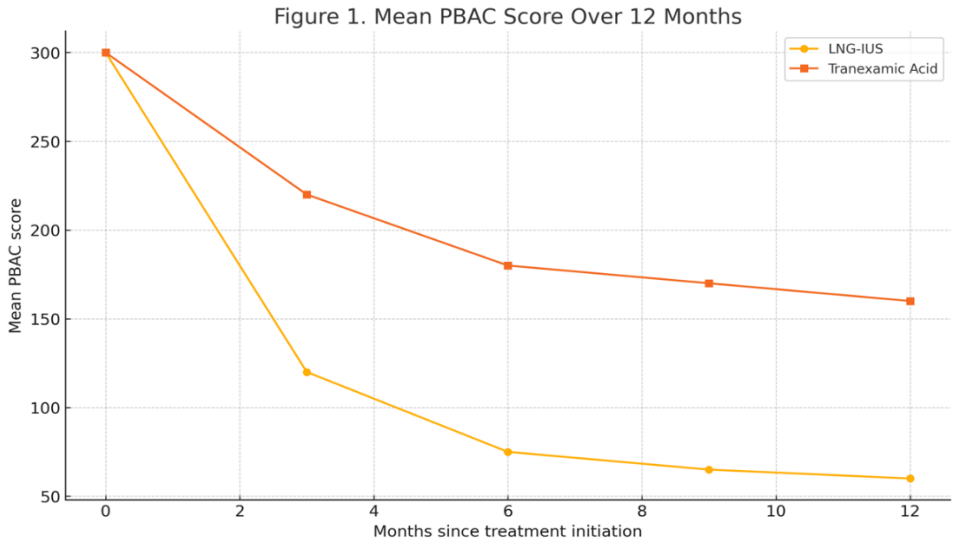

Figure 1: Mean PBAC score over 12 months

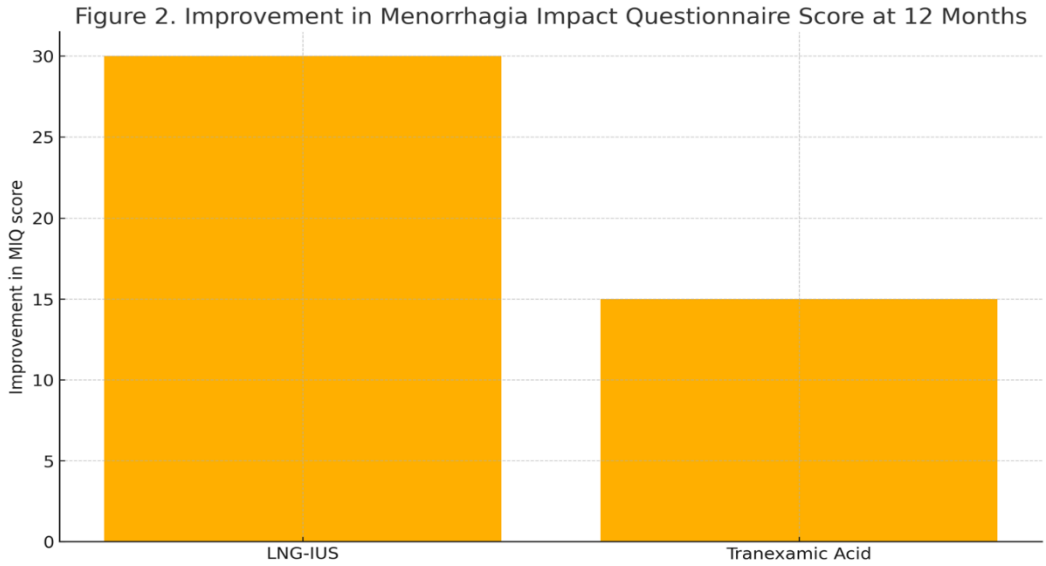

Figure 2: Improvement in Menorrhagia Impact Questionnaire score at 12 months

Discussion

This pragmatic RCT shows that, in perimenopausal women, LNG IUS offers substantial improvements in menstrual blood loss and better gains in haemoglobin, ferritin and quality of life, at 12 months than cyclic oral TXA. The 100 point reduction of the PBAC is more than the 30 point minimal clinically important difference [9] and replicates previous indirect comparisons at mixed age cohorts [5, 10]. Results in our study add to previously existing evidence that among perimenopause cases, anovulatory bleeding and comorbidities may limit their reactions to systemic therapies.

LNG-IUS yielded amenorrhoea in 58 %, comparable to 55-65 % reported in previous trials [11], while only 12 % of TXA users achieved similar control, aligning with pooled estimates of 15 % [11,12,13]. The local progestogenic action of LNG-IUS induces profound endometrial suppression regardless of ovulatory status, explaining its consistent efficacy. TXA acts via antifibrinolysis and is limited to active dosing days; higher baseline plasmin activity in perimenopausal endometrium may partially account for diminished effect. Notably, haemoglobin rose by almost 2 g/dL with LNG-IUS, reflecting near elimination of bleeding and superior iron repletion, whereas TXA's modest improvement mirrors its partial blood-loss reduction. Improved MIQ scores underscore the broader functional benefits of LNG-IUS, including reduced work impairment and social limitation.[14-16] Safety profiles were reassuring. Device expulsion (4 %) and hormonal side-effects were infrequent and similar to published rates [17-18]. The single superficial thrombophlebitis under TXA echoes meta-analytic data showing no significant thrombotic excess [17-18], yet vigilance remains warranted, especially in older or obese women. Strengths include multicentre design, objective blood-loss quantification and robust follow-up. Limitations encompass open-label allocation, potential self-report bias in PBAC diaries, and exclusion of large fibroids and lack of cost-effectiveness analysis. Generalizability is limited to women without desire for future fertility.[19-22] Our data support current guideline hierarchies that place LNG-IUS as first-line therapy but uniquely quantify the magnitude of benefit over TXA in perimenopause. For women preferring non-hormonal or episodic control, TXA remains effective yet less potent. Shared decision-making should incorporate individual tolerance for hormonal exposure, required bleeding control and risk factors for thromboembolism. Future research should evaluate comparative cost-utility and long-term (> 24 months) continuation beyond the perimenopausal transition.

Conclusion

Levonorgestrel releasing intra uterine system is substantially more effective, and clinically so, than cyclic oral tranexamic acid in perimenopausal women with heavy menstrual bleeding in blood loss, correction of anaemia and improvements in quality of life with low rate of complication. There is thus reason to recommend LNG IUS as the method of choice in terms of a preferred first line medical therapy of HMB in the context of fulfilling their contraceptive requirements. Tranexamic acid can be considered a viable episodic option in women who refuse or are unable to use hormonal devices but the efficacy should be tempered. A long term analysis of its cost effectiveness coupled with extensions past the 24 months mark is desirable.

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