



Comparison of Intramuscular Dose of Progesterone with Oral Progesterone in Heavy Menstrual Bleeding

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ABSTRACT

Objective: To compare the efficacy of oral and intramuscular progesterone in women with heavy menstrual bleeding presenting at tertiary care hospital. **Methodology:** The aim of this investigation was to rigorously assess the comparative impacts of oral versus intramuscular administration of progesterone in a cohort of females aged 18 to 49 experiencing significant menstrual hemorrhage; this study was undertaken at the Department of Obstetrics and Gynaecology, Sheikh Zayed Woman Hospital, SMBBMU, Larkana, during the period from November, 2024 to April, 2025. Subjects were systematically assigned to receive either oral or intramuscular progesterone through a randomized protocol across three distinct cycles. The assessment of therapeutic efficacy was performed at the three-month interval. The data obtained were analyzed through the software SPSS version 26.0, considering $P \leq 0.05$ as significant. **Results:** The average age of the subjects was 31.13 ± 7.85 years in the oral administration group, and 32.81 ± 7.56 years in the intramuscular group. The therapeutic effectiveness was observed in 37.7% of females who were given oral progesterone, in contrast to just 15.1% of those who were treated with intramuscular progesterone. This observed variance was determined to be statistically significant ($p = 0.008$). **Conclusion:** Current findings reveal that oral progesterone shows significantly enhanced effectiveness relative to intramuscular progesterone in addressing menorrhagia among women within the reproductive age group. In light of its superior effectiveness and convenient administration, oral progesterone ought to be regarded as a preferential therapeutic modality. These results furnish empirically supported guidance for the judicious selection of the most advantageous route of progesterone therapy within clinical practice.

INTRODUCTION

Heavy menstrual bleeding (HMB), also termed menorrhagia, signifies a major gynecological complication, influencing an estimated 20% of women within the reproductive age category. [1]. In medical discourse, HMB is identified by menstrual blood loss (MBL) of ≥ 80 mL per cycle, a benchmark that was set in pioneering studies carried out by Hallberg et al. [2]. The PALM-COEIN classification system developed by International Federation of Gynecology and Obstetrics (FIGO) classifies the putative etiologies responsible for determining the causal factors in abnormal uterine bleeding (AUB) in a systematic way structure-based (PALM) and nonstructure-based (COEIN) [3].

HMB has a vital function in defining the quality of life among women, playing a part in conditions including anemia, low energy, and limitations in social and job-related activities [4-5]. Progestogens are frequently used to treat heavy menstrual bleeding (HMB), particularly when the preservation of fertility is important or surgical

methods are contraindicated. In an endometrium that has received estrogen priming, progesterone drives the transition from a proliferative to a secretory phase by activating progesterone receptors A and B [6]. The effectiveness of progestogens is contingent upon a myriad of factors, encompassing the method of administration, metabolic stability, half-life, and receptor affinity [7,8]. Additionally, their ability to decidualize and thin the endometrial lining plays a key role in reducing menstrual blood loss [9].

Although a number of therapeutic options are available, the levonorgestrel-releasing intrauterine system (LNG-IUS) remains the best non-invasive treatment for heavy menstrual bleeding (HMB) supported by significant evidence from randomized controlled trials and systematic reviews [10,11]. However, LNG-IUS may not be suitable for all patients due to cost, insertion-related discomfort, or contraindications such as distorted uterine anatomy or active pelvic infection [12]. Oral progestogens are widely prescribed, yet their efficacy in reducing MBL,

particularly when used for short durations during the luteal phase, has shown inconsistency in clinical trials [13]. Yildiz et al. compared oral and vaginal progesterone and found similar improvements in cycle regularity between the two groups [14]. Likewise, a study conducted in a tertiary care hospital in A comprehensive systematic review indicated that intrauterine and injectable progestogens resulted in more significant decreases in menstrual blood loss and enhancements in hemoglobin levels relative to oral progestogens among women experiencing heavy menstrual bleeding [15]. HMB has additionally been linked to adverse psychosocial and economic repercussions, thereby underscoring the necessity for efficacious and readily available management strategies. [16,17].

Although several studies have examined oral and intrauterine progesterone, there is a significant lack of data regarding the use of intramuscular progesterone for the treatment of HMB. Intramuscular formulations may present certain benefits including enhanced patient adherence, prolonged hormone concentrations, and evasion of hepatic first-pass metabolism [18,19]. Although progesterone serves multiple roles in gynecological treatments, a distinct absence of studies directly comparing intramuscular and oral forms in addressing heavy menstrual bleeding (HMB) reveals a critical void in current academic work.

Consequently, the current investigation was formulated to evaluate the comparative effectiveness of oral and intramuscular progesterone in females exhibiting heavy menstrual bleeding within a tertiary care medical facility. The results aspire to offer clinical recommendations regarding the most advantageous method of progesterone delivery to enhance outcomes for women impacted by this prevalent and incapacitating condition.

METHODOLOGY

This randomized controlled trial was conducted at the Department of Obstetrics and Gynaecology, Sheikh Zayed Woman Hospital, SMBBMU, Larkana, from November, 2024 to April, 2025. The study involved women aged 18 to 49 years presenting with heavy menstrual bleeding, defined as menstrual bleeding lasting more than seven days, requiring frequent pad or tampon changes, or passing clots the size of a quarter or larger. Treatment was considered effective if all signs of heavy menstrual bleeding resolved within three months of therapy. Participants were selected through non-probability consecutive sampling. Women with known coagulopathies, other gynecological or systemic causes of abnormal bleeding, on anticoagulant therapy, pregnant or lactating, with severe chronic illnesses, prior hysterectomy, or uterine abnormalities were excluded from the study. Eligible participants who met the inclusion criteria were recruited from the outpatient department after informed consent was obtained. Demographic and clinical details were recorded using a structured proforma. Participants were randomly assigned to receive either oral progesterone 400 mg daily from the 15th to the 25th day of the cycle for three consecutive cycles, or intramuscular progesterone 20 mg once daily over the same period, using an opaque sealed envelope technique. All participants

were followed for three months to evaluate treatment efficacy of the treatment. Data were entered and analyzed using SPSS version 26.0; means and standard deviations were calculated for continuous variables, while frequencies and percentages were computed for categorical variables, with Chi-square test applied to compare treatment outcomes consider $P \leq 0.05$ as criteria of statistical significance.

RESULTS

A comprehensive overview of the notable characteristics of the participants incorporated in the study is presented in Table 1 (group A, n=53; group B, n=53). Within Group A, the mean chronological age was determined to be 31.13 ± 7.85 years, whereas in Group B it was assessed at 32.81 ± 7.56 years. The mean body mass index (BMI) in Group A was quantified at $25.76 \pm 3.43 \text{ kg/m}^2$, in contrast to the figure of $24.82 \pm 3.68 \text{ kg/m}^2$ observed in Group B. Furthermore, Group A exhibited prolonged durations of heavy menstrual bleeding (HMB), averaging 8.32 ± 1.88 days, when compared to Group B, which reported an average of 6.77 ± 1.52 days. In a similar vein, the hemoglobin (Hb) concentration was found to be lower in Group A ($10.39 \pm 0.81 \text{ mg/dL}$) as opposed to Group B ($11.12 \pm 1.01 \text{ mg/dL}$). With respect to residential status, a substantial proportion of participants in Group A were classified as urban residents (66.0%), in contrast to 45.3% within Group B, while rural residency was predominantly observed in Group B (54.7%) compared to Group A (34.0%). The socioeconomic status exhibited minimal disparity between the two groups, with the middle class representing the most prevalent category in both groups (47.2% in Group A and 39.6% in Group B). The distribution of lower and upper classes appeared to be relatively consistent across both groups.

The comparative effectiveness of oral (Group A) and intramuscular (Group B) progesterone in a sample of women with significant menstrual bleeding is presented in Table 2. Within Group A, 20 out of 53 women (37.7%) showed a favorable therapeutic response, whereas in group B efficacy was noted in 8(15.1%) women. In contrast, a greater proportion of individuals within Group B (84.9%) were categorized as non-effective responders when juxtaposed with Group A (62.3%). This observed divergence in therapeutic efficacy between the two cohorts was determined to be statistically significant, with a p-value of 0.008, thereby indicating that oral progesterone manifested superior effectiveness in relation to intramuscular progesterone within the confines of this particular study population.

Table 1
Characteristics of Study Patients (n=106)

Characteristics of Participants	Groups	
	A (n=53)	B (n=53)
Age in years, Mean ± SD	31.13 ± 7.85	32.81 ± 7.56
BMI in kg/m ² , Mean ± SD	25.76 ± 3.43	24.82 ± 3.68
Duration of Heavy menstrual bleeding in days	8.32 ± 1.88	6.77 ± 1.52
HB Level in mg/dl, Mean ± SD	10.39 ± 0.81	11.12 ± 1.01
Residential status, n (%)	Urban	35 (66.0)
	Rural	18 (34.0)
Socioeconomic Status, n (%)	Lower Class	12 (22.6)
	Middle Class	25 (47.2)
	Upper Class	16 (30.2)

Table 2

Comparison of Treatment Efficacy Between Oral and Intramuscular Progesterone in Women with Heavy Menstrual Bleeding (n=106)

Efficacy, n (%)	Group		P-Value
	A (n=53)	B (n=53)	
Effective	20 (37.7%)	8 (15.1%)	0.008
Non-Effective	33 (62.3%)	45 (84.9%)	

DISCUSSION

We conducted this study to compare the efficacy of oral versus intramuscular progesterone for the treatment of heavy menstrual bleeding (HMB). Oral progesterone was therefore found to have an efficacy rate of 37.7% while efficacy with intramuscular progesterone was only 15.1%, with a statistically significant p-value of 0.008. These findings imply that oral progesterone may provide enhanced symptom management and improved clinical outcomes for women experiencing HMB. Heavy menstrual bleeding (HMB) continues to be one of the most common gynecological complaints, affecting as many as 20% of women of reproductive age and may be the cause of anemia, impaired quality of life and psychological distress [1,2]. To facilitate etiological diagnosis of abnormal uterine bleeding (AUB) and to exclude any secondary causes before starting a hormonal treatment, FIGO developed the PALMCOEIN classification [3]. Among the medical therapies, the levonorgestrel-releasing intrauterine system (LNG-IUS) is first-line, with regular risk-of-bias-adjusted systematic reviews and clinical trials demonstrating its consistent ability to reduce menorrhagia [10,11]. Nevertheless, there exists a subset of patients who are unable to utilize the LNG-IUS owing to challenges related to insertion or anomalies in uterine morphology [12]. Oral progestogens are frequently advocated for the treatment of menorrhagia; nonetheless, their efficacy has shown inconsistency across various studies, especially when administered intermittently during the luteal phase [13]. In agreement with the previous research by Yildiz et al. [14], oral and vaginal progesterone had similar effects on inducing a menstrual cycle and indicating that the route or means of administration may be secondary to systemic absorption [14]. Furthermore, a systematic review by Abdel-Aleem et al. found that injectable and intrauterine progestogens were generally more effective than oral forms in reducing

menstrual blood loss and improving hemoglobin levels [15]. In contrast to that review, our study focused specifically on the intramuscular route, which, despite its theoretical advantages such as bypassing hepatic first-pass metabolism and achieving prolonged serum levels [18,19], demonstrated lower clinical efficacy than the oral route. The disparity between the expected pharmacological benefits of intramuscular progesterone and its observed clinical effectiveness may be clarified by a variety of determinants. These determinants include insufficient dosing, variable tissue absorption, or patient-related factors such as delayed follow-up and suboptimal tolerability. Moreover, the augmented effectiveness of oral progesterone identified in our study may be attributed to improved cycle regulation achieved through its administration during the luteal phase over three successive cycles. This research possesses the merits of a randomized controlled design coupled with a direct comparative analysis between oral and intramuscular progesterone in the context of heavy menstrual bleeding, a domain that remains relatively underexplored. Nevertheless, the main limitations are the small number of patients, the resolution of the symptoms was based on the clinical lifetime without quantitative objects, such as the Pictorial Blood Loss Assessment Chart (PBAC) [16] and the absence of endometrial histopathological examination. The present investigation elucidates that oral progesterone exhibits superior efficacy compared to intramuscular progesterone in mitigating excessive menstrual bleeding. These results yield novel understandings pertaining to the choice of progesterone therapy and advocate for the sustained use of oral progesterone as a more practical and effective substitute in the standard clinical approach to heavy menstrual bleeding (HMB).

CONCLUSION

Current findings reveal that oral progesterone shows significantly enhanced effectiveness relative to intramuscular progesterone in addressing menorrhagia among women within the reproductive age group. In light of its superior effectiveness and convenient administration, oral progesterone ought to be regarded as a preferential therapeutic modality. These results furnish empirically supported guidance for the judicious selection of the most advantageous route of progesterone therapy within clinical practice.

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