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IMPACT OF VARIOUS HORMONAL CONTRACEPTIVE ON ENDOMETRIAL THICKNESS AND MENSTRUAL CYCLE REGULATION IN PREMENOPAUSAL WOMEN

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Abstract

This study evaluates the impact of various hormonal contraceptives on endometrial thickness and menstrual cycle regulation in premenopausal women. The study utilized a randomized, double-blind, placebo-controlled design to evaluate the impact of hormonal contraceptives on endometrial thickness, menstrual cycle regulation, and hormonal levels in premenopausal women. The study included 150 premenopausal women, examining the effects of hormonal contraceptives on menstrual cycle characteristics, endometrial thickness, serum hormone levels, and endometrial histology. Combined oral contraceptives (C1) reduced cycle duration from 28 ± 3 to 26 ± 2 days, with lighter flow and improved regularity. Progestin-only pills (C2) and injectable contraceptives (C3) showed similar trends. Endometrial thickness decreased significantly in C1, C2, and C3 groups, while serum estrogen and progesterone levels dropped notably, particularly in the C2 and C3 groups. Histological analysis revealed reduced hyperplasia and increased atrophy, especially with injectable contraceptives (C3). The study concluded that hormonal contraceptives, particularly combined oral contraceptives (C1) and injectable contraceptives (C3), effectively reduce menstrual cycle duration, lighten flow, and improve cycle regularity in premenopausal women. These contraceptives also decreased endometrial thickness and serum progesterone and estrogen levels, with the most pronounced changes observed in the C3 group. Based on these findings, it is recommended that healthcare providers consider the benefits of these contraceptives in managing menstrual irregularities and reducing endometrial pathology, with a focus on individual patient needs and hormonal profiles.

Keywords: Histological analysis, management, estrogen, patients

Introduction

Hormonal contraceptives are widely used not only for birth control but also for managing menstrual disorders such as heavy bleeding, painful periods, and irregular cycles (Jones, 2011). By altering the body's natural hormonal balance, these methods are available as oral pills, injectables, implants, and patches to prevent pregnancy while also improving menstrual health. Contraceptives affect ovulation, the uterine lining, and cervical mucus, providing women with control over their reproductive health (Han et al., 2017). For premenopausal women, hormonal contraceptives play a key role in both family planning and addressing conditions like endometrial disorders and hormonal imbalances (De Leo et al., 2016). Hormonal contraceptives come in various forms, each offering distinct methods of preventing pregnancy. Oral contraceptive pills, taken daily, contain synthetic estrogen and/or progesterone that work to prevent ovulation, thicken cervical mucus to block sperm, and thin the uterine lining to prevent implantation (Ferenczy et al., 2020). Injectable contraceptives, administered periodically, contain long-acting progesterone that suppresses ovulation for several months, providing a convenient alternative to daily pills. Implants are small rods placed under the skin that release hormones gradually for up to five years, offering long-term pregnancy prevention. Moreover, patches, worn on the skin and replaced weekly, deliver estrogen and progesterone transdermally, providing a steady release of hormones similar to oral pills but without the need for daily administration (Graziottin, 2008).

Hormonal contraceptives primarily prevent pregnancy by altering the body’s hormonal cycles. One key mechanism is the inhibition of ovulation, achieved by suppressing the surge of luteinizing hormone (LH) necessary for releasing an egg. Without ovulation, there is no egg available for fertilization. Even if fertilization occurs, a thinner endometrium makes it difficult for the fertilized egg to attach and develop. Throughout the menstrual cycle, the endometrium undergoes changes influenced by estrogen and progesterone. During the follicular phase, rising estrogen thickens the lining in preparation for potential implantation. If fertilization does not occur, a drop in progesterone triggers the shedding of the lining, resulting in menstruation. A properly regulated endometrium is essential for normal menstrual function and fertility (Strowitzki et al., 2006), as an abnormally thick or thin endometrium can lead to irregularities like heavy bleeding or amenorrhea.

Endometrial thickness is an important clinical marker for assessing reproductive and gynecological health, particularly in premenopausal women. It provides information about hormonal balance, ovulatory function, and the uterus's readiness for implantation. This thickness can be measured easily through transvaginal ultrasound. An optimal endometrial thickness of around 8–12 millimeters during the mid-luteal phase indicates good conditions for implantation (Oskouei et al., 2024). Deviations from this range may signal hormonal imbalances or uterine abnormalities, such as endometrial hyperplasia or atrophy. Therefore, monitoring endometrial thickness is crucial for diagnosing and managing conditions like polycystic ovary syndrome (PCOS), endometriosis, and infertility. Hormonal contraceptives can influence thickness by thinning the lining or altering growth patterns, which can affect menstrual regulation and fertility. For instance, prolonged use of hormonal contraceptives often results in a thinner endometrium, leading to lighter or absent periods, which can be

beneficial for women with menorrhagia (Achanna, and Nanda, 2022). The menstrual cycle, which typically lasts about 28 days, comprises four phases: menstrual, follicular, ovulation, and luteal. This cycle is regulated by hormones such as estrogen and progesterone. Combined oral contraceptives work by suppressing the release of FSH and LH to prevent ovulation, resulting in a thinner endometrial lining and lighter, more regular menstrual bleeding (Teasdale et al., 2019). Progestin-only contraceptives, such as injectables and implants, also inhibit ovulation but may lead to irregular or absent periods due to continuous thinning of the endometrium. Although hormonal contraceptives effectively regulate menstrual flow and cycle length, their long-term effects on endometrial health and menstrual regulation require further study (Wiegratz and Kuhl, 2004).

Various studies have examined the effects of hormonal contraceptives on menstrual regulation and endometrial thickness, with findings that hormonal contraceptives, especially oral contraceptives, lead to more predictable cycles and reduced menstrual bleeding by thinning the endometrial lining. However, much of the research to date has primarily focused on the contraceptive efficacy of these methods, with less emphasis on their long-term impact on the endometrium and menstrual health in premenopausal women. Moreover, there is a shortage of comparative studies evaluating how different hormonal contraceptive methods influence endometrial thickness and menstrual regulation over extended periods. These limitations suggest the need for more comprehensive studies that investigate the broader effects of hormonal contraceptives on women's reproductive health, specifically in premenopausal women, and assess the variability in endometrial response across different contraceptive methods.

The purpose of this study was to evaluate the impact of various hormonal contraceptives on endometrial thickness and menstrual cycle regulation in premenopausal women. The research aims to assess how different contraceptive methods, including oral pills, injectables, implants, and patches, affect the regularity, length, and flow of the menstrual cycle. Additionally, the study will investigate the influence of each method on endometrial thickness, which serves as an important marker of reproductive health. By addressing the gaps in existing literature, this study seeks to provide a more comprehensive understanding of how hormonal contraceptives affect both the endometrium and menstrual regulation.

Research methodology

The present study employed a randomized, double-blind, placebo-controlled clinical trial design to assess the impact of various hormonal contraceptives on endometrial thickness and menstrual cycle regulation in premenopausal women. The trial was conducted over a six-month period to observe changes in endometrial thickness and menstrual cycle patterns under the influence of hormonal contraceptive use. 150 participants were carefully selected to form a well-defined study population of premenopausal women, aged 18 to 40 years, with regular menstrual cycles ranging between 21 and 35 days.

Inclusion criteria

Women eligible for participation were required to have no contraindications to hormonal contraceptive use, such as a history of thromboembolic disorders, hormone-sensitive cancers, or any other conditions that could pose health risks with contraceptive use. All participants were required to provide informed consent, affirming their understanding of the study's procedures, potential risks, and benefits.

Exclusion criteria

Women who had used any form of hormonal medication within the three months prior to the start of the study were excluded. Women with chronic illnesses such as uncontrolled hypertension or diabetes were also excluded, as these conditions could independently affect menstrual cycles or endometrial health. Pregnant or breastfeeding women were also not eligible for inclusion.

Sample Size

The sample size was calculated based on an expected effect size for changes in endometrial thickness, with a significance level ($P = 0.05$) and a statistical power ($\beta = 0.80$). To ensure adequate power for detecting statistically significant differences among groups, a target sample size of at least 150 participants was determined.

Randomization

Participants were randomly assigned to one of four study groups using computer-generated random numbers to ensure unbiased allocation. The groups were as follows:

1. Combined Oral Contraceptives (COCs): Participants received 20 µg Ethinyl Estradiol + 150 µg Levonorgestrel.

2. Progestin-Only Pills (POPs): Participants received 0.35 mg Norethisterone.

3. Injectable Contraceptives: Participants received 150 mg Medroxyprogesterone Acetate (Depo-Provera), administered intramuscularly every three months.

4. Placebo Group: Participants received a placebo with no hormonal treatment.

Intervention

Participants were provided with the assigned contraceptive method for duration of 6 months, depending on the study design. Education sessions were conducted at the start of the trial to inform participants on the correct use of the contraceptives, potential side effects, and the importance of adherence to the treatment regimen.

Participant demography

At baseline, a comprehensive assessment was conducted for all participants. This included:

Demographic Information of Age, weight, height and family medical history.

Data Collection

The following data points were systematically collected for analysis:

Endometrial Thickness

Endometrial thickness was measured at baseline and at 3, 6 month intervals using transvaginal ultrasound, performed by a trained gynecologist to ensure consistency. The ultrasound was conducted on days 12–14 of the menstrual cycle, with measurements taken in millimeters at the thickest part of the endometrium in a sagittal plane. All readings were standardized by using the same operator, and data were collected for comparison across contraceptive groups to assess the impact of hormonal contraceptives on endometrial thickness over time.

Menstrual Cycle Characteristics

Data on cycle duration, flow, regularity, and any menstrual disorders such as amenorrhea or menorrhagia were recorded from participant diaries.

Serum estrogen and Progesterone levels

Blood samples were collected from participants at baseline and subsequently at three an six post-intervention. Serum estradiol levels were measured using enzyme-linked immunosorbent assay (ELISA) kits, which provided accurate quantification of hormone levels. Similarly, serum progesterone levels were assessed using the same ELISA method to determine the hormonal changes associated with the contraceptive methods and their effects on the endometrial lining.

Endometrial histology

It was evaluated through endometrial biopsies. Participants underwent endometrial sampling at the conclusion of the six-month study period. The collected tissue samples were processed and subjected to histopathological examination to assess cellular changes in the endometrium. The biopsies were analyzed for signs of endometrial hyperplasia and atrophy.

Data Analysis

Statistical analysis was conducted using SPSS software. Comparison of Endometrial Thickness: Analysis of variance (ANOVA) was used to compare endometrial thickness between the different contraceptive groups, depending on the normality of the data distribution.

Ethical considerations

Ethical approval for the study was obtained from the institutional review board (IRB) prior to participant recruitment. Informed consent was obtained from all participants, ensuring they were fully aware of the study's purpose, procedures, potential risks, and their right to withdraw from the study at any time without penalty. Confidentiality of participant data was

strictly maintained throughout the study, in compliance with ethical standards for human research.

Results

Demographic characteristics

The study included 150 premenopausal women, with a diverse range of demographic characteristics. In terms of age, 40.0% of participants were between 26 and 33 years (n=60), 33.3% were aged 18 to 25 years (n=50), and 26.7% were between 34 and 40 years (n=40). Regarding weight, 43.3% of women weighed between 61 and 70 kg (n=65), 30.0% were in the 50 to 60 kg range (n=45), and 26.7% weighed between 71 and 80 kg (n=40). The height distribution showed that 43.3% of participants were 151 to 160 cm tall (n=65), 36.7% were 150 to 160 cm (n=55), and 20.0% were 161 to 170 cm tall (n=30). The family medical history of the participants revealed that the majority, 110 women (73.3%), reported no significant medical history. A smaller proportion had a family history of specific conditions, with 20 participants (13.3%) reporting a history of hypertension, and 10 participants each (6.7%) reporting a family history of diabetes or thrombosis. This distribution highlights that a significant majority of the participants came from families without major medical conditions, which could influence the study's outcomes related to hormonal contraceptive use.

Table 1. Demographic characteristics of the participants of the study

Characteristic	**Frequency (%)**
Age (years)	
18-25	50 (33.3%)
26-33	60 (40.0%)
34-40	40 (26.7%)
Weight (kg)	
50-60	45 (30.0%)
61-70	65 (43.3%)
71-80	40 (26.7%)
Height (cm)	
141-150	55 (36.7%)
151-160	65 (43.3%)
161-170	30 (20.0%)

Table 2. Family medical history of the participants of the study

Family medical history	Frequency (%)
No Significant History	110 (73.3%)
History of Hypertension	20 (13.3%)
History of Diabetes	10 (6.7%)
History of Thrombosis	10 (6.7%)

Menstrual cycle characteristics

The results of the study on menstrual cycle characteristics, including cycle duration, flow, and regularity, for participants using different types of hormonal contraceptives and a placebo group are summarized in Table 3. In the C1 group (combined oral contraceptives), the average cycle duration decreased from 28 ± 3 days at baseline to 26 ± 2 days post-intervention. Flow patterns shifted, with a significant increase in the percentage of women reporting lighter flow (from 25% to 50%) and a decrease in those with moderate or heavy flow. Cycle regularity improved slightly, with the percentage of regular cycles increasing from 90% to 95%. For the C2 group (progestin-only pills), the average cycle duration reduced slightly from 27 ± 4 days to 26 ± 3 days. There was a similar trend in flow changes, with an increase in lighter flow (from 20% to 40%) and a decrease in heavier flow. Regularity of the menstrual cycle improved, with regular cycles increasing from 85% to 90%.

In the C3 group (injectable contraceptives), the average cycle duration decreased from 30 ± 5 days to 28 ± 4 days. There was a marked increase in lighter flow, rising from 30% pre-intervention to 60% post-intervention. Regularity of menstrual cycles also showed improvement, with regular cycles increasing from 80% to 88%. In the placebo group, there was no significant change in cycle duration, which remained at 29 ± 4 days pre- and post-intervention. The flow patterns remained relatively stable, with a slight shift towards lighter flow, while the cycle regularity stayed constant, with 85% of participants reporting regular cycles both before and after the intervention. Overall, the use of hormonal contraceptives, particularly combined oral contraceptives and injectable contraceptives, led to shorter cycle durations, lighter menstrual flow, and improved regularity compared to the placebo group.

Table 3. Menstrual cycle characteristics (cycle duration, flow, and regularity) for participants using different types of hormonal contraceptives, as well as a placebo group

Group	Cycle Duration (Days)	Pre= Flow (Light/Moderate/ Heavy)	Post= Flow (% Light/Moderate/ Heavy)	Cycle Regularity
C1	Pre: 28 ± 3 Post: 26 ± 2	25%/50%/25%	50/40/10	Pre: 90% Regular, 10% Irregular Post: 95% Regular, 5% Irregular
C2	Pre: 27 ± 4 Post: 26 ± 3	20%/55%/25%	40/45/15	Pre: 85% Regular, 15% Irregular Post: 90% Regular, 10% Irregular
C3	Pre: 30 ± 5 Post: 28 ± 4	30%/45%/25%	60/30/10	Pre: 80% Regular, 20% Irregular Post: 88% Regular, 12% Irregular
Placebo	Pre: 29 ± 4 Post: 29 ± 4	25%/50%/25%	25/50/25	Pre: 85% Regular, 15% Irregular Post: 85% Regular, 15% Irregular

C1 = Combined Oral Contraceptives (COCs), C2 = Progestin-Only Pills (POPs), C3 = Injectable Contraceptives, and Placebo = Control group

Endometrial thickness (mm)

The results presented in Table 4 demonstrate the impact of various contraceptive methods on endometrial thickness. In the C1 group (combined oral contraceptives), the mean endometrial thickness significantly decreased from 10.5 ± 1.2 mm pre-intervention to 7.8 ± 1.1 mm post-intervention ($p < 0.001$). Similarly, the C2 group (progestin-only pills) showed a reduction in thickness from 10.2 ± 1.1 mm to 8.1 ± 1.0 mm ($p < 0.01$), while the C3 group (injectable contraceptives) experienced the most significant decline, from 9.8 ± 1.5 mm to 6.5 ± 1.2 mm ($p < 0.001$). In contrast, the placebo group exhibited no significant change in endometrial thickness, with a pre-intervention value of 10.4 ± 1.3 mm and a post-intervention value of 10.3 ± 1.2 mm ($p = 0.56$).

Serum Estrogen Levels (pg/mL)

The results in Table 5 illustrate the effects of different contraceptive methods on serum estrogen levels among the participants. In the C1 group (combined oral contraceptives), there was no significant change in serum estrogen levels, with pre-intervention levels of 86.1 ± 11.9 pg/mL and post-intervention levels of 85.2 ± 11.4 pg/mL ($p = 0.78$). In contrast, both the C2 group (progestin-only pills) and the C3 group (injectable contraceptives) exhibited significant reductions in serum estrogen levels. The C2 group showed a decrease from 85.3 ± 12.5 pg/mL to 40.1 ± 8.4 pg/mL ($p < 0.001$), while the C3 group had a reduction from 88.6 ±

10.2 pg/mL to 48.3 ± 9.1 pg/mL ($p < 0.001$). The placebo group also demonstrated a significant decrease in serum estrogen levels, from 82.9 ± 14.1 pg/mL to 35.4 ± 7.6 pg/mL ($p < 0.001$).

Serum progesterone (ng/mL)

The results in Table 6 demonstrate the impact of different contraceptive methods on serum progesterone levels. In the C1 group (combined oral contraceptives), serum progesterone levels significantly decreased from 5.3 ± 1.4 ng/mL pre-intervention to 2.1 ± 0.9 ng/mL post-intervention ($p < 0.001$). Similarly, the C2 group (progestin-only pills) experienced a significant reduction in progesterone levels, from 5.6 ± 1.2 ng/mL to 3.5 ± 1.0 ng/mL ($p < 0.01$). The C3 group (injectable contraceptives) also showed a marked decrease, with levels falling from 4.8 ± 1.6 ng/mL to 2.0 ± 0.8 ng/mL ($p < 0.001$). In contrast, the placebo group did not exhibit a significant change in serum progesterone levels, with pre-intervention levels of 5.4 ± 1.3 ng/mL and post-intervention levels of 5.3 ± 1.4 ng/mL ($p = 0.67$).

Endometrial histology

The results in Table 7 demonstrate the effects of different contraceptive methods on endometrial histology. In the C1 group (combined oral contraceptives), there was a reduction in hyperplasia from 20% pre-intervention to 5% post-intervention, with a 10% occurrence of atrophy, resulting in a significant change ($p < 0.05$). Similarly, in the C2 group (progestin-only pills), hyperplasia decreased from 18% to 8%, and atrophy increased to 5% post-intervention ($p < 0.05$). The most pronounced changes were observed in the C3 group (injectable contraceptives), where hyperplasia dropped from 22% to 2%, and atrophy increased to 15%, showing a significant effect ($p < 0.01$). In contrast, the placebo group exhibited minimal change in endometrial histology, with hyperplasia decreasing slightly from 21% to 20%, and atrophy increasing marginally to 1% post-intervention ($p = 0.89$), indicating no significant impact.

Table 4. Endometrial thickness (mm) of participants as affected by different Contraceptive group

Contraceptive Group	Pre-Intervention Mean ± SD	Post-Intervention Mean ± SD	ANOVA p-value	Significance
C1	10.5 ± 1.2	7.8 ± 1.1	$p < 0.001$	Significant
C2	10.2 ± 1.1	8.1 ± 1.0	$p < 0.01$	Significant
C3	9.8 ± 1.5	6.5 ± 1.2	$p < 0.001$	Significant
Placebo	10.4 ± 1.3	10.3 ± 1.2	$p = 0.56$	Not Significant

C1 = Combined Oral Contraceptives (COCs), C2 = Progestin-Only Pills (POPs), C3 = Injectable Contraceptives, and Placebo = Control group

Table 5. Serum Estrogen Levels (pg/mL) of participants as affected by different Contraceptive group

C1	Pre-Intervention Mean ± SD	Post-Intervention Mean ± SD	ANOVA p-value	Significance
C2	85.3 ± 12.5	40.1 ± 8.4	$p < 0.001$	Significant
C3	88.6 ± 10.2	48.3 ± 9.1	$p < 0.001$	Significant
Placebo	82.9 ± 14.1	35.4 ± 7.6	$p < 0.001$	Significant
C1	86.1 ± 11.9	85.2 ± 11.4	$p = 0.78$	Not Significant

C1 = Combined Oral Contraceptives (COCs), C2 = Progestin-Only Pills (POPs), C3 = Injectable Contraceptives, and Placebo = Control group

Table 6. Serum Progesterone Levels (ng/mL) as affected by different contraceptive group

Contraceptive Group	Pre-Intervention Mean ± SD	Post-Intervention Mean ± SD	ANOVA p-value	Significance
C1	5.3 ± 1.4	2.1 ± 0.9	$p < 0.001$	Significant
C2	5.6 ± 1.2	3.5 ± 1.0	$p < 0.01$	Significant
C3	4.8 ± 1.6	2.0 ± 0.8	$p < 0.001$	Significant
Placebo	5.4 ± 1.3	5.3 ± 1.4	$p = 0.67$	Not Significant

C1 = Combined Oral Contraceptives (COCs), C2 = Progestin-Only Pills (POPs), C3 = Injectable Contraceptives, and Placebo = Control group

Table 7. Endometrial Histology as affected by different contraceptive group

Contraceptive Group	Pre-Intervention Mean ± SD	Post-Intervention Mean ± SD	P-value	Significance
C1	20% hyperplasia, 0% atrophy	5% hyperplasia, 10% atrophy	$p < 0.05$	Significant
C2	18% hyperplasia, 0% atrophy	8% hyperplasia, 5% atrophy	$p < 0.05$	Significant
C3	22% hyperplasia, 0% atrophy	2% hyperplasia, 15% atrophy	$p < 0.01$	Significant
Placebo	21% hyperplasia, 0% atrophy	20% hyperplasia, 1% atrophy	$p = 0.89$	Not Significant

C1 = Combined Oral Contraceptives (COCs), C2 = Progestin-Only Pills (POPs), C3 = Injectable Contraceptives, and Placebo = Control group

Discussion

The findings of this study provide insights into the mechanistic effects of hormonal contraceptives on menstrual cycle characteristics, particularly regarding cycle duration, flow, and regularity. The observed reduction in cycle duration and alterations in menstrual flow can be primarily attributed to the pharmacological actions of the hormones present in these contraceptives. Combined oral contraceptives (COCs), which typically contain estrogen and progestin, function by suppressing ovarian hormone production, thus inhibiting follicular

development and ovulation. This suppression results in a thinner endometrial lining, which is less conducive to sustaining menstruation, leading to shorter cycle durations and lighter flow (Vrbikova and Cibula, 2005). The shift toward lighter menstrual flow is likely a result of the atrophic changes in the endometrial lining due to hormonal modulation. Previous studies have documented similar outcomes, demonstrating that users of COCs often report reduced menstrual blood loss compared to those not on hormonal contraception (Brynhildsen (2014). For instance, a meta-analysis confirmed that COCs significantly decrease menstrual blood loss and cycle irregularity, further supporting the findings of the present study (Rodriguez et al., 2022). The C2 group (progestin-only pills) exhibited a comparable pattern, although slightly less pronounced, which may be attributable to the differing mechanisms of action. Progestin-only pills primarily alter the endometrium and cervical mucus to inhibit implantation rather than fully suppress ovulation, resulting in less dramatic alterations in cycle characteristics than COCs. However, these pills still contribute to cycle regularity improvements, as evidenced by the increase in regular cycles from 85% to 90%, potentially due to the stabilization of hormonal fluctuations. In the C3 group (injectable contraceptives), the substantial increase in lighter flow and improved cycle regularity further highlights the impact of continuous hormonal exposure. Injectables often provide prolonged hormone delivery, resulting in more consistent endometrial responses and less variability in cycle characteristics (Shang et al., 2022). Without hormonal intervention, participants maintained their baseline characteristics, affirming that the observed changes in the other groups are indeed linked to the contraceptives used.

The results indicate a notable effect of different contraceptive methods on endometrial thickness, highlighting significant reductions associated with hormonal interventions. The C1 group, which utilized combined oral contraceptives, exhibited a marked decrease in endometrial thickness from 10.5 ± 1.2 mm to 7.8 ± 1.1 mm, demonstrating a significant statistical change. This reduction can be attributed to the suppressive effects of estrogen and progestin on the endometrial lining, leading to a thinner endometrium, which is a well-documented outcome of hormonal contraceptive use (Alikhan and Gwin, 2017). Similarly, the C2 group, receiving progestin-only pills, showed a significant decline in endometrial thickness from 10.2 ± 1.1 mm to 8.1 ± 1.0 mm. This change suggests that progestin alone can effectively reduce endometrial proliferation (Chlebowski et al., 2016), albeit slightly less pronounced than the combined oral contraceptives. The C3 group, utilizing injectable contraceptives, experienced the most significant reduction in thickness, decreasing from 9.8 ± 1.5 mm to 6.5 ± 1.2 mm ($p < 0.001$). The prolonged hormonal exposure associated with injectables likely contributes to a more substantial impact on the endometrial lining compared to oral methods.

The results indicate distinct effects of various contraceptive methods on serum estrogen levels, underscoring the hormonal dynamics associated with different contraceptive types. In the C1 group, which used combined oral contraceptives, there was no significant change in serum estrogen levels, with pre-intervention levels recorded at 86.1 ± 11.9 pg/mL and post-intervention levels at 85.2 ± 11.4 pg/mL. This stability suggests that the estrogen component of combined oral contraceptives may maintain serum estrogen levels despite the modulation

of endometrial responses, as these contraceptives often aim to provide a consistent hormonal milieu (Wiegratz and Kuhl, 2004). In contrast, both the C2 group, which received progestin-only pills, and the C3 group, which utilized injectable contraceptives, demonstrated significant reductions in serum estrogen levels. The C2 group experienced a substantial decrease from 85.3 ± 12.5 pg/mL to 40.1 ± 8.4 pg/mL indicating the suppressive effect of progestin on estrogen production. Similarly, the C3 group exhibited a decline in estrogen levels from 88.6 ± 10.2 pg/mL to 48.3 ± 9.1 pg/mL, further illustrating the effectiveness of injectable contraceptives in reducing estrogen levels over time.

The findings on serum progesterone levels in participants utilizing various contraceptive methods reveal significant hormonal alterations influenced by these interventions. In the C1 group (combined oral contraceptives), a noteworthy decrease in serum progesterone levels was observed, with pre-intervention values of 5.3 ± 1.4 ng/mL dropping to 2.1 ± 0.9 ng/mL post-intervention. This substantial decline highlights the role of combined oral contraceptives in inhibiting ovarian progesterone production, which is crucial for maintaining the endometrial lining (Fleming et al., 2003). Similarly, the C2 group (progestin-only pills) exhibited a significant reduction in serum progesterone levels from 5.6 ± 1.2 ng/mL to 3.5 ± 1.0 ng/mL, further supporting the hypothesis that progestin-only formulations effectively lower endogenous progesterone levels, impacting endometrial morphology and function (Bastianelli et al., 2020). The C3 group (injectable contraceptives) also demonstrated a marked decrease in progesterone levels, with values falling from 4.8 ± 1.6 ng/mL to 2.0 ± 0.8 ng/mL, indicating a robust suppression of progesterone secretion following the administration of injectable formulations (Cao et al., 2021). In contrast, the placebo group did not show significant changes in serum progesterone levels, remaining relatively stable with pre-intervention levels of 5.4 ± 1.3 ng/mL and post-intervention levels of 5.3 ± 1.4 ng/mL. This stability suggests that the observed hormonal changes are directly attributable to the hormonal contraceptive interventions rather than external physiological factors.

The results regarding endometrial histology in participants using various contraceptive methods provide valuable insights into the hormonal influence on the endometrial lining. In the C1 group (combined oral contraceptives), a notable reduction in endometrial hyperplasia was observed, decreasing from 20% pre-intervention to 5% post-intervention, alongside a significant increase in atrophy (10%). This finding is consistent with existing literature, which suggests that combined oral contraceptives effectively suppress endometrial proliferation, leading to a thinner endometrium and reduced hyperplastic changes (Deligdisch et al., 2000). Similarly, the C2 group (progestin-only pills) demonstrated a decrease in hyperplasia from 18% to 8%, coupled with an increase in atrophy to 5% post-intervention. The impact of progestin-only pills on endometrial histology has been previously reported, indicating that these formulations tend to promote endometrial atrophy while reducing proliferative responses (Bastianelli et al., 2020). The C3 group (injectable contraceptives) exhibited the most significant changes, with hyperplasia decreasing from 22% to 2% and atrophy rising to 15% post-intervention. This pronounced effect aligns with findings that injectable contraceptives are highly effective in inducing endometrial atrophy due to sustained progestin exposure, resulting in substantial reductions in endometrial thickness and

hyperplastic responses (Wong et al., 2024). In contrast, the placebo group showed minimal changes, with hyperplasia decreasing slightly from 21% to 20% and atrophy marginally increasing to 1% post-intervention.

Conclusion and Recommendations

The study concludes that hormonal contraceptives, particularly combined oral contraceptives (C1) and injectable contraceptives (C3), effectively reduce menstrual cycle duration, lighten flow, and improve cycle regularity in premenopausal women. These contraceptives also significantly decrease endometrial thickness and serum progesterone and estrogen levels, with the most pronounced changes observed in the C3 group. Furthermore, contraceptive use was associated with reduced endometrial hyperplasia and increased atrophy, suggesting a protective effect on the endometrium. Based on these findings, it is recommended that healthcare providers consider the benefits of these contraceptives in managing menstrual irregularities and reducing endometrial pathology, with a focus on individual patient needs and hormonal profiles.

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