OPEN ACCESS

Kashf Journal of Multidisciplinary Research
Vol: 01 - Issue 12 (2024)
P-ISSN: 3007-1992 E-ISSN: 3007-200X
https://kjmr.com.pk

SYNTHETIC CONTRACEPTIVES AND THEIR IMPACT ON ENDOMETRIAL THICKNESS AND MENSTRUAL CYCLE REGULATION IN REPRODUCTIVE-AGE WOMEN

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Article Info

Abstract
The trial investigated the influence of various synthetic contraceptives on endometrial thickness and menstrual cycle regulation in reproductive-age women using a randomized, double-blind, placebo-controlled design. A total of 150 participants were evaluated for changes in menstrual cycle patterns, endometrial thickness, serum hormone levels, and endometrial histology. Combined oral contraceptives (C1) reduced cycle length from 28 ± 3 to 26 ± 2 days, resulting in lighter flow and improved regularity, while similar trends were observed with progestin-only pills (C2) and injectable contraceptives (C3). Significant reductions in endometrial thickness were noted across all groups, accompanied by marked decreases in serum estrogen and progesterone levels, particularly in the C2 and C3 groups. Histological analysis revealed reduced hyperplasia and increased endometrial atrophy, most prominently in the C3 group. Overall, hormonal contraceptives, particularly C1 and C3, effectively shortened cycle duration, regulated flow, and reduced endometrial thickness and hormone levels, with the most pronounced effects observed in the C3 group. These findings suggest that synthetic contraceptives are valuable options for managing menstrual irregularities and reducing endometrial abnormalities, emphasizing the need for personalized treatment based on individual hormonal profiles and clinical needs.

Keywords: *Histological analysis, management, estrogen, patients*

Introduction

Synthetic contraceptives are used not only for birth control but also to treat menstrual disorders like heavy bleeding, painful periods, and irregular cycles (Jones, 2011). These methods are available as oral pills, injectables, implants, and patches to prevent pregnancy while improving menstrual health by altering the body's natural hormonal balance. Contraceptives alter ovulation, the uterine lining, and cervical mucus, giving women control over their reproductive health (Han et al., 2017). For premenopausal women, Synthetic contraceptives play a central role in family planning as well as in the treatment of conditions such as endometrial disorders and hormonal imbalances (De Leo et al., 2016).

Synthetic 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).

Synthetic 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 serves as a crucial clinical indicator for evaluating reproductive and gynecological health, particularly in premenopausal women. It offers insights into hormonal balance, ovulatory function, and the uterus's preparedness for implantation. This thickness can be easily measured using transvaginal ultrasound. An optimal endometrial thickness of approximately 8–12 millimeters during the mid-luteal phase suggests favorable conditions for implantation (Oskouei et al., 2024). Deviations outside this range may indicate hormonal imbalances or uterine issues, such as endometrial hyperplasia or atrophy. As such, monitoring endometrial thickness is essential for diagnosing and managing conditions like polycystic ovary syndrome (PCOS), endometriosis, and infertility. Synthetic contraceptives can impact endometrial thickness by thinning the uterine lining or altering its growth patterns, which in turn can influence menstrual regulation and fertility. For example, prolonged use of synthetic contraceptives often results in a thinner endometrium, causing lighter or absent periods, which can be beneficial for women with menorrhagia (Achanna & Nanda, 2022). The menstrual cycle, typically lasting 28 days, consists of four phases: menstrual, follicular, ovulation, and luteal, regulated by hormones like estrogen and progesterone. Combined oral contraceptives prevent ovulation by suppressing the release of FSH and LH, leading to a thinner endometrial lining and more regular, lighter menstrual bleeding (Teasdale et al., 2019). Progestin-only contraceptives, including injectables and implants, also inhibit ovulation but may result in irregular or absent

periods due to continuous thinning of the endometrium. Nevertheless, synthetic contraceptives effectively regulate menstrual flow and cycle; their long-term effects on endometrial health and menstrual regulation require further study (Wiegratz and Kuhl, 2004).

While several studies have explored the effects of synthetic contraceptives on menstrual regulation and endometrial thickness, most have focused on contraceptive efficacy rather than the long-term impact on the endometrium and menstrual health in premenopausal women. Additionally, there is a lack of comparative studies on how different contraceptive methods affect endometrial thickness and menstrual cycles over time. These gaps highlight the need for more comprehensive research on the broader effects of synthetic contraceptives on reproductive health in premenopausal women. This study aims to assess the effects of various synthetic contraceptives on endometrial thickness and menstrual cycle regulation in premenopausal women. Specifically, it will examine how methods such as oral pills, implants and patches influence menstrual cycle characteristics, including regularity, duration, and flow. The research will also explore the impact of these contraceptives on endometrial thickness, a key indicator of reproductive health. Moreover, this study seeks to provide a clearer understanding of how synthetic contraceptives affect both the endometrium and menstrual cycle regulation.

Methodology

The present study employed a randomized, double-blind, placebo-controlled clinical trial design to assess the impact of different 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 and Exclusion criteria

Women eligible for participation had to be free of contraindications to any contraceptive use, i.e. a history of thromboembolic disorders, hormone-sensitive cancers, or other health risks associated with contraceptive use. Participants were required to provide informed consent, acknowledging their understanding of the study's procedures, risks, and benefits. Exclusion criteria included recent use of hormonal medications (within three months), chronic illnesses like uncontrolled hypertension or diabetes, and pregnancy or breastfeeding, as these factors could impact menstrual cycles or endometrial health.

Sample Size

The sample size was measured based on a predictable 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 demonstrated.

Randomization

Members 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 given the assigned contraceptive method for duration of 6 months, in accordance with the study design. At the start of the trial, education sessions were held to instruct participants on the proper use of the contraceptives, potential side effects, and the importance of adhering to the treatment regimen.

Demographic Characteristics

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 Synthetic 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

Endometrial biopsies were performed to evaluate the condition of the endometrium. At the end of the six-month study, participants underwent endometrial sampling. The tissue samples were processed and examined histopathologically to identify cellular changes in the endometrium, including 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 was granted by the institutional review board (IRB) before recruiting participants. Informed consent was obtained from all participants, ensuring they understood purpose of the study, procedures, potential risks, and their right to withdraw at any time without consequence. Participant data confidentiality was maintained throughout the study, following ethical guidelines 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.

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 Synthetic 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 results of this study offer valuable insights into the effects of synthetic contraceptives on menstrual cycle characteristics, particularly cycle duration, flow, and regularity. The reduction in cycle duration and changes in menstrual flow can mainly be attributed to the hormonal actions of these contraceptives. Combined oral contraceptives (COCs), which typically contain estrogen and progestin, work by suppressing ovarian hormone production, thereby inhibiting follicular development and ovulation. This suppression leads to a thinner endometrial lining, making it less capable of sustaining menstruation, which results in shorter cycles and lighter flow (Vrbikova and Cibula, 2005). The reduction in menstrual flow is likely due to atrophic changes in the endometrial lining induced by hormonal modulation. Similar findings have been reported in previous studies, which show that COC users often experience reduced menstrual blood loss compared to non-users of 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) showed a similar trend, though the effects were less pronounced, likely due to the different mechanisms of action. Progestin-only pills primarily affect the endometrium and cervical mucus to prevent implantation, rather than fully suppressing ovulation, resulting in less dramatic changes in cycle characteristics compared to COCs. Nonetheless, these pills still contributed to improved cycle regularity, with regular cycles increasing from 85% to 90%, possibly due to reduced hormonal fluctuations. In the C3 group (injectable contraceptives), the significant increase in lighter flow and better cycle regularity further emphasized the impact of continuous hormonal exposure. Injectable contraceptives provide sustained hormone delivery, leading to more stable endometrial responses and less variability in cycle characteristics (Shang et al., 2022). Participants not using hormonal methods maintained their baseline characteristics, confirming that the observed changes in the other groups were indeed related to the contraceptives used.

The results also revealed a significant reduction in endometrial thickness across different contraceptive methods. The C1 group, which used combined oral contraceptives, showed a notable decrease in endometrial thickness from 10.5 ± 1.2 mm to 7.8 ± 1.1 mm, representing a statistically significant 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 injectable likely contributes to a more substantial impact on the endometrial lining compared to oral methods.

The results highlight the different effects of contraceptive methods on serum estrogen levels, reflecting the hormonal changes associated with each type. In the C1 group, which used combined oral contraceptives (COCs), serum estrogen levels remained largely unchanged. Pre-intervention levels were 86.1 ± 11.9 pg/mL, and post-intervention levels were 85.2 ± 11.4 pg/mL, showing little fluctuation. This suggests that the estrogen in COCs helps maintain steady estrogen levels in the bloodstream, even as it alters endometrial responses, as these contraceptives are designed to maintain a consistent hormonal environment (Wiegratz and Kuhl, 2004). In contrast, both the C2 group (progestin-only pills) and the C3 group (injectable contraceptives) saw significant reductions in serum estrogen levels. The C2 group experienced a sharp drop from 85.3 ± 12.5 pg/mL to 40.1 ± 8.4 pg/mL, indicating that progestin suppresses estrogen production. Similarly, the C3 group showed a decrease from 88.6 ± 10.2 pg/mL to 48.3 ± 9.1 pg/mL, further demonstrating the ability of injectable contraceptives to lower 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 endometrial histology results revealed significant changes in response to different contraceptive methods. In the C1 group (combined oral contraceptives), endometrial hyperplasia decreased from 20% to 5%, while atrophy increased to 10%, indicating effective suppression of endometrial proliferation (Deligdisch et al., 2000). In the C2 group (progestin-only pills), hyperplasia decreased from 18% to 8%, and atrophy increased to 5%, consistent with previous reports of progestin-induced endometrial atrophy (Bastianelli et al., 2020). The C3 group (injectable contraceptives) showed the most pronounced changes, with hyperplasia dropping from 22% to 2% and atrophy rising to 15%, reflecting the strong atrophic effects of sustained progestin exposure

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

Conclusion and Recommendations

The study achieves that synthetic contraceptives, especially combined oral contraceptives (C1) and injectable contraceptives (C3), reduce menstrual cycle duration, improve cycle regularity and lighten flow in premenopausal women. These contraceptives also decrease endometrial thickness, estrogen levels and serum progesterone, 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 results, it is indorsed 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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