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Comparing clinical performance of two-rod levonorgestrel implants across brands: A three-year multicenter randomized clinical trial on Sinoplant and Indoplant

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ABSTRACT

Objective: To compare the effectiveness, safety, acceptability, and confounding factors of the two-rod levonorgestrel implants between the Indoplant and Sinoplant implant brands.**Methods:** The study was a double-blind, randomized controlled trial at three different centers in Indonesia. A total of 531 participants that met inclusion and exclusion criteria were randomized into two groups, with 264 participants in the Sinoplant group and 267 participants in the Indoplant group. At each center, participants were divided into two groups for Sinoplant and Indoplant. The participants were followed up for 36 months. Four parameters were evaluated: implant effectiveness, safety, acceptability, and confounding factors.**Results:** A total of 531 eligible participants were enrolled in this study. Both Sinoplant and Indoplant showed 100% efficacy in preventing pregnancy, with no significant differences in side effects. 24.22% of the Sinoplant group and 22.18% of the Indoplant group reported weight changes. 8.60% of the Sinoplant group and 9.73% of the Indoplant group reported menstrual changes, and 1.17% of the both groups experienced intermenstrual bleeding. Implant acceptability was 96.61%, with 3.39% dropout rates. Confounding factors such as age, parity, and contraceptive history did not significantly differ between the two groups.**Conclusions:** Sinoplant and Indoplant did not differ significantly in contraceptive effectiveness, safety, acceptability, and confounding factors.**KEYWORDS:** Contraceptives; Implants; Levonorgestrel; Effectiveness; Acceptability; Side effects

1. Introduction

Long-acting reversible contraceptive methods are effective for pregnancy prevention. These methods include etonogestrel implants,

copper intrauterine devices (IUDs), and levonorgestrel implants. Long-acting reversible contraceptives are highly popular in Indonesia, which ranks among the top users of implants, particularly the two-rod levonorgestrel implant. Levonorgestrel, a synthetic progestin derived from 19-nortestosterone, is administered either as a single formulation or in combination with ethinyl estradiol in oral contraceptives. Comparative studies have demonstrated that levonorgestrel implants exhibit lower failure rates and one-year pregnancy rates compared to oral contraceptives and IUDs.

Indoplant, a locally developed generic implant, is widely used but has not been systematically compared with other brands. The aim

Key Points

Question: How do Sinoplant and Indoplant compare in clinical performance over three years?**Findings:** Both implants (Sinoplant and Indoplant) showed high effectiveness, similar safety profiles, and high continuation rates.**Meaning:** Sinoplant and Indoplant are equally reliable options for long-term contraception, supporting their broader use in family planning programs.

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of this study was to compare the effectiveness, safety, and acceptability of Indoplant with the branded Sinoplant and to identify contributing factors. We hypothesized that there would be no significant differences across these outcomes.

Indoplant and Sinoplant are both two-rod subdermal contraceptive implants containing 150 mg of levonorgestrel, offering up to 3 years of effective pregnancy prevention through ovulation suppression, cervical mucus thickening, and endometrial changes. Sinoplant inhibits ovulation, as evidenced by progesterone levels exceeding 9.5 nmol/L. This mechanism prevents ovarian follicle enlargement, leading to anovulatory cycles. Additionally, Sinoplant thickens cervical mucus, further hindering sperm penetration. No clinical changes have been reported in liver, kidney, adrenal gland, or steroid function among users of this contraceptive implant[1]. A four-year study of two-rod levonorgestrel implants revealed a cumulative pregnancy rate of 0.001, no significant difference in continuation rates, and menstrual disturbances as the most common side effect. The serum levonorgestrel level in Indoplant also did not significantly differ from that in the Sinoplant group[2].

They share similar side effects such as menstrual irregularities, headaches, breast tenderness, weight changes, and mood swings. The most common side effect of Indoplant (a three-year two-rods implant) is menstrual disturbances. This effect is strongly associated with a rapid decline in serum levonorgestrel levels. After 24 hours, basal levonorgestrel levels are lower in the Indoplant group than in the Sinoplant group. The serum levonorgestrel level in Indoplant (649.6 pmol/L) corresponds to the non-ovulatory threshold at 48 months and does not significantly differ from that in the Sinoplant group (758.8 pmol/L)[2]. The key differences lie in their origin and regulatory status: Indoplant is a locally manufactured in Indonesia, while Sinoplant is imported from China.

2. Methods

2.1. Study design

This study was a parallel, multicenter, double-blind randomized controlled trial (RCT) with a 1:1 allocation ratio between Sinoplant and Indoplant implants, conducted at three different centers in three different cities across Indonesia: Universitas Gadjah Mada in Yogyakarta, Universitas Sumatera Utara in Medan, and Universitas Airlangga in Surabaya. Participants were randomly assigned to two groups using permuted block randomization method. One group received the branded Sinoplant, while the other received the generic Indoplant (a three-year two-rod implant).

2.2. Randomization procedure

Randomization was conducted using the Clinical Trial Management System, developed by Human Reproduction Programme conducted by the World Health Organization (HRP-WHO). Eligible participants were randomly assigned to either the Sinoplant or Indoplant group. Block randomization was employed, with each block

comprising ten participants. The principal investigator generated the random allocation sequence. Midwives at each center enrolled participants, and assignments to interventions were performed blindly. Within each block, a separate randomization process allocated five participants to Sinoplant and five to Indoplant. The order of participant numbers and group assignments was determined by randomization. Each assignment was then placed in a sealed envelope, numbered sequentially from 1 to 600. When a participant met the inclusion criteria, satisfied exclusion criteria, and had a normal Visual Inspection with Acetic Acid (IVA) examination, an envelope was opened in sequence. The IVA examination was carried out to confirm that participants had no other conditions that might interfere with the study. The participants were then assigned to the corresponding group based on the envelope contents. Consequently, all participants, midwives, and research teams were blinded after assignment. An open-label event was conducted in 2024 after all study procedures were completed.

2.3. Study parameters

This study evaluated the effectiveness, safety, acceptability of the implants, along with factors influencing these outcomes. Effectiveness was assessed through clinical signs, reported symptoms, and urine pregnancy tests. During follow-up visits, participants were specifically queried about complaints such as headaches, dizziness, acne, vaginal bleeding patterns, lower abdominal pain, and overall health status to assess safety and acceptability. Acceptability was evaluated by assessing satisfaction, dropout rates, and reasons for withdrawal. Reasons for implant/IUD removal included medical factors (expulsion, bleeding, and other medical indications) as well as personal factors (desire for pregnancy, relocation, and other reasons). Significant confounding factors influencing the effectiveness, safety, and acceptability of Sinoplant compared to Indoplant were analyzed quantitatively.

2.4. Participant recruitment

Participants were recruited from October 4, 2017 to May 5, 2018 at three centers (Yogyakarta, Medan, and Surabaya), with 180 participants enrolled at each site. The open label process was conducted at the end of 2024 following a 2-year extension research.

The participant flow of the study is presented in Figure 1. The targeted number of participants was 540. Then, a total of 531 participants that met inclusion and exclusion criteria were randomized into two groups, with 264 participants in the Sinoplant group and 267 participants in the Indoplant group. The sample size was calculated using Pocock's "Equivalence Trial" formula. The calculation assumed a three-year survival rate of 97%, a significance level of 5%, a power (1- β) of 90%, and an equivalence tolerance of 5%. Additionally, a dropout rate of 10% was considered. Thus, the required sample size was calculated as 240–270 participants per group. Random allocation of participants was implemented to minimize heterogeneity in confounding factors.

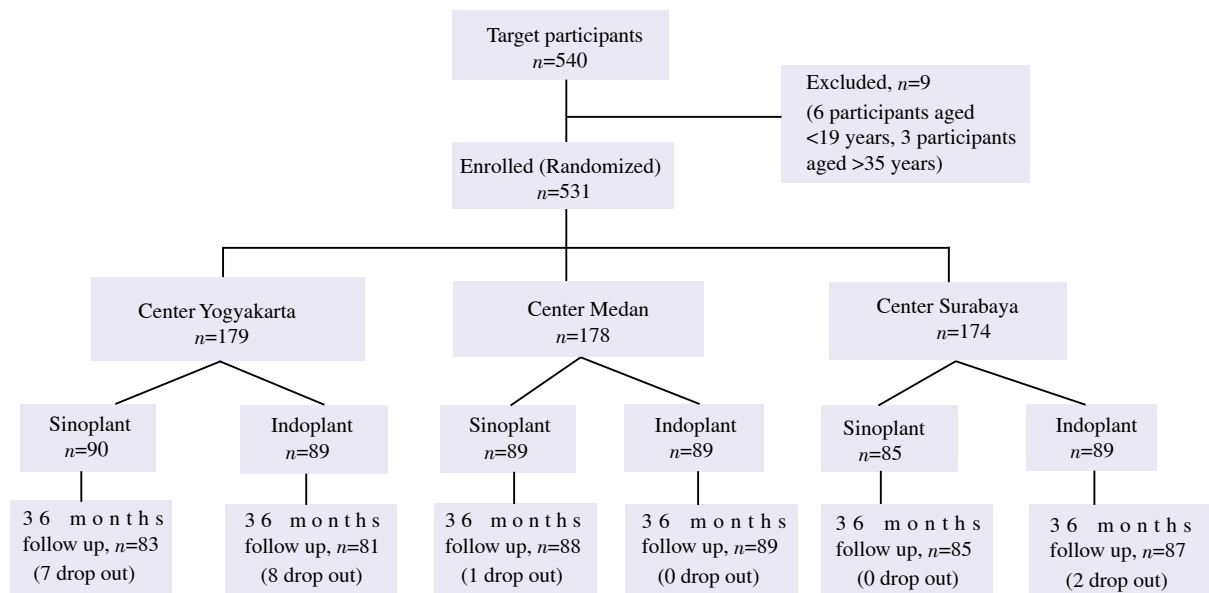


Figure 1. Participant flow of the study.

2.5. Data collection

Informed consent was obtained from women aged 20–35 years seeking a contraceptive method, after they received comprehensive information about the study, including randomization, implant insertion and removal procedures, study objectives, and potential risks and benefits. Eligible women who voluntarily agreed to participate signed an informed consent form. Follow-up assessments were conducted for three years or until accidental pregnancy, implant/IUD removal, or participant withdrawal, whichever occurred first.

2.6. Inclusion, exclusion and drop out criteria

Participants were eligible if they met all of the following criteria: (1) healthy fertile women aged 20–35 years old; (2) not pregnant; (3) having a normal menstrual cycle; (4) new users of hormonal contraception or users of non-hormonal contraception (IUD, condoms, or other natural contraceptive methods). Women switching from another contraceptive must have completed a “washout period” of at least three months and resumed a normal menstrual cycle; (5) currently sexually active and at risk of pregnancy; (6) not exposed to hormonal contraception in the last three months; (7) having received and understood the study explanation, including its purpose, risks, and benefits, and having signed informed consent; (8) willing to return to the clinic for follow-up visits; (9) willing to use the implant for at least three years.

Women were excluded if they had any of the following: (1) absolute contraindications to hormonal contraception, including thrombophlebitis, thromboembolic, hypertension, cerebrovascular accident, liver disease, known or suspected breast or genital cancer, or suspected estrogen-dependent neoplasia; (2) anemia; (3) pregnancy; (4) obesity (Broca Index >60%); (5) currently under hormonal treatment, including estrogen, progesterone, or thyroid hormone therapy; (6) history or occurrence of pelvic inflammatory disease; (7) total amenorrhea >1 year during implant or hormonal

contraceptive use; (8) treatment with non-hormonal drugs affecting contraceptive pharmacodynamics, including chronic diseases such as tuberculosis, systemic lupus erythematosus, chronic liver disease; (9) family history of cancer; (10) abnormal or undiagnosed genital bleeding; (11) thromboembolism or severe cardiovascular disease; (12) current or recent use of liver enzyme-inducing drugs (*e.g.*, barbiturates, phenytoin, carbamazepine, rifampicin); (13) hypertension (systolic >160 mmHg, diastolic >100 mmHg); (14) severe hirsutism; or (15) participation in another clinical trial in the past three months.

Each participant had the right to withdraw at any time, and investigators were required to honor this decision. Reasons for withdrawal included: (1) personal reasons, such as planning pregnancy; (2) clinical reasons, including serious side effects or adverse events; (3) relocation that prevented follow-up; (4) investigator decision. Participants were immediately withdrawn if they: (1) became pregnant; (2) experienced migraines with prolonged dizziness; (3) developed a significant blood pressure increase (diastolic > 15 mmHg, systolic > 30 mmHg); or (4) reported intolerable side effects or pain.

The principal investigator, sponsor, and research coordinator conducted periodic monitoring to assess compliance with study protocols, procedures, regulations, and Good Clinical Practice (GCP) guidelines. Monitoring included verification of document completeness, storage, recruitment procedures, and Case Report Form (CRF) entries in accordance with the protocol and GCP standards. For participants lost to follow-up or with missing data, investigators attempted to recontact them through the site coordinator or directly, documenting the reasons, including withdrawal decisions. Participants who withdrew or had missing data were documented in the CRF, including the reasons, in accordance with withdrawal criteria.

2.7. Statistical analysis

SPSS Version 15 (IBM) was used, and the normality of numerical data was assessed using Kolmogorov-Smirnov test. Univariate

analysis was performed to describe participant characteristics. Bivariate analysis was performed to examine changes in clinical assessments (weight and blood pressure). *Chi square test*, Fisher's test, and Mann-Whitney test were used. The relationship between several factors and the implant group variables was also analyzed. Data in the study were presented as mean±standard deviation (mean±SD), *n*(%), or median (min-max). Data were considered statistically significant at $P<0.05$.

2.8. Ethics statement

This study received ethical approval from multiple committees: (1) BKKBN Research Ethics Committee for Family Planning and Reproductive Health (Number 2434/PD.101/H4/2015, on October 19, 2015); (2) BKKBN Research Ethics Committee for Family Planning and Reproductive Health (Number 1466/PL.301/H4/2017, on May 23, 2017); (3) Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Public Health and Nursing, Gadjah Mada University (KE/FK/0733/EC/207, on July 6, 2017); (4) approval for clinical trial implementation (Number B-PN.01.06.313.3.12.16.9772, on December 19, 2016); (5) Sinoplant Clinical Trial Centre Move (Number PN.01.06.313.3.07.17.3111, on July 3, 2017).

3. Results

3.1. Participants' baseline data

A total of 531 eligible participants were enrolled in this study, with 264 in the Sinoplant group and 267 in the Indoplant group. The median age was 28 years (range: 19-38) in the Sinoplant group and 29 years (range: 18-36) in the Indoplant group. Median blood pressure in the Sinoplant group was 110 (range: 80-150) mmHg systolic and 70 (range: 60-100) mmHg diastolic, while in the Indoplant group it was 110 (range: 90-140) mmHg systolic and 70 (range: 60-90) mmHg diastolic. Median body weight was 56 (range: 34-170) kg in the Sinoplant group and 57 (range: 34-86) kg in the Indoplant group. Nearly half of the participants expressed a desire to have another child after the study. Median of the menstrual cycle length was 28 (range: 21-50) days in the Sinoplant group and 28 (range: 14-32) days in the Indoplant group. Baseline data showed no significant differences between groups ($P>0.05$).

Before enrollment, the three-month injection was the most common contraceptive method in both groups, followed by condoms and pills. Data related to participants' health conditions, menstrual patterns, pregnancy, post-insertion complaints, body weight, and blood pressure were collected during visits from 0 to 36 months. Most participants in both groups discontinued prior contraception due to expiration, desire for pregnancy, menstrual disorders linked to injectables, concerns about contraceptive failure, or inconvenience. Most participants reported no history of excessive bleeding (>7 days), intermenstrual bleeding, cycles >35 or <21 days, amenorrhea >3 months, or severe dysmenorrhea requiring medication. In their most recent cycle, most participants reported menstrual duration of

fewer than eight days. Participant characteristics are described in Table 1.

3.2. Follow up after 36 months of implant insertion

3.2.1. Clinical parameters after 36 months of implant insertion

After 36-month follow-up, some participants dropped out. Consequently, 256 participants were in the Sinoplant group and 257 participants were in the Indoplant group. Three clinical parameters were analyzed after 36 months of implant insertion: (1) body weight, (2) systolic blood pressure, and (3) diastolic blood pressure. The median body weight in the Sinoplant group was 60 kg (range: 35–85 kg), while in the Indoplant group it was 60 kg (range: 24–86 kg). No significant difference in body weight was observed between baseline and 36-month follow-up ($P=0.23$). At 36 months, the median systolic blood pressure was 110 mmHg in both groups (range: 80–178 mmHg for Sinoplant; 90–156 mmHg for Indoplant). No significant difference in systolic blood pressure was found between baseline and 36 months ($P=0.67$). At 36 months, the median diastolic blood pressure was 70 mmHg in both groups (range: 30–107 mmHg for Sinoplant; 60–100 mmHg for Indoplant). No significant difference in diastolic blood pressure was observed between baseline and 36 months ($P=0.57$). All clinical parameters after 36 months of implant insertion are summarized in Table 2.

3.2.2. Participants' health conditions at the 36-month follow-up

At 36 months, systolic blood pressure was (112.88±9.55) mmHg in the Sinoplant group and (112.25±8.92) mmHg in the Indoplant group ($P=0.43$). Diastolic blood pressure was (73.96±7.19) mmHg in the Sinoplant group and (74.61±6.89) mmHg in the Indoplant group ($P=0.51$). However, the average frequency of sexual intercourse per week differed significantly between the two groups at 36 months ($P<0.05$). Participants' health conditions at the 36-month follow-up are summarized in Table 3.

3.2.3. Menstrual pattern of the subjects at the 36-month follow-up

At the 36-month follow-up, menstrual pattern parameters included the occurrence of menstruation after implant placement, number of cycles, bleeding outside the expected period, duration of bleeding, and presence of excessive bleeding. 90.64% participants had menstruation after implant placement. For these parameters, no significant differences were observed between the two groups. Menstrual patterns at the 36-month follow-up are shown in Table 4.

At the 36-month visit, urine-based pregnancy tests indicated that all participants tested negative, as shown in Table 5.

3.2.4. Post implant insertion complaints

32.75% of the participants reported some complaints, including dizziness/headache, nausea/vomiting, facial spots/acne, weight changes, decreased sexual desire, alterations in the menstrual patterns, spotting, and visual disturbances. However, no significant differences were found between Sinoplant and Indoplant groups in relation to these complaints (all $P>0.05$). Post-insertion complaint data are shown in Table 6.

4. Discussion

The study found 100% pregnancy prevention over 36 months with both Sinoplant and Indoplant, consistent with global data on levonorgestrel implants. A systematic review reported a Pearl Index below 1 for etonogestrel subdermal implants, indicating high contraceptive efficacy[3]. Similarly, a study in Brazil found that the etonogestrel implant showed higher contraceptive effectiveness than short-acting reversible contraceptives, with continuation rates of

89.9% at one year and 75.4% at two years[4].

Participants in this study reported various complaints, including weight changes and alterations in menstrual patterns, but no significant differences were found between Sinoplant and Indoplant. A 2019 study examining weight gain associated with levonorgestrel and etonogestrel implants over a 12-month period found significantly greater weight gain in the levonorgestrel group than in the etonogestrel group[5]. These findings were further supported by a multicenter clinical trial conducted at 12 research locations across

Table 1. Baseline characteristics of participants ($n=531$).

Characteristics	Implant types	
	Sinoplant, $n=264$	Indoplant, $n=267$
Demographics		
Age, years, median (min-max)	28 (19-38)	29 (18-36)
Education, $n(\%)$		
No formal education	1 (0.38)	1 (0.37)
Elementary school	12 (4.55)	15 (5.62)
Junior high school	80 (30.30)	59 (22.10)
Senior high school	147 (55.68)	164 (61.42)
College	24 (9.09)	28 (10.49)
Occupation, $n(\%)$		
Not working/Housewife	165 (62.50)	174 (65.17)
Civil servant	3 (1.14)	4 (1.50)
Private employee	56 (21.21)	53 (19.85)
Self-employed	20 (7.57)	19 (7.12)
Services (Tailor/pedicab driver/laborer, etc.)	11 (4.17)	7 (2.62)
Farmer	7 (2.65)	7 (2.62)
Other	2 (0.76)	3 (1.22)
Religion, $n(\%)$		
Islam	231 (87.50)	234 (87.64)
Catholic	6 (2.27)	10 (3.75)
Cristian	26 (9.85)	22 (8.24)
Hindu	1 (0.38)	1 (0.37)
Vital sign, median (min-max)		
Body height, cm	155.0 (139-170)	154.5 (100-190)
Body weight, kg	56 (34-170)	57 (34-86)
Upper arm circumference, cm	27 (20 -38)	27 (20-35)
Systolic blood pressure, mmHg	110 (80-150)	110 (90-140)
Diastolic blood pressure, mmHg	70 (60-100)	70 (60-90)
Heart rate, times/minute	80 (26-110)	80 (50-120)
Respiration rate, times/minute	20 (12-28)	20 (12-24)
Obstetric history and contraceptive use		
Number of children, median (min-max)	2 (1-6)	2 (1-5)
Desire to have another child, $n(\%)$		
Yes	131 (49.62)	132 (49.44)
No	133 (50.38)	135 (50.56)
Sexual intercourse, times/week, median (min-max)	2 (1-5)	2 (1-7)
Prior use of contraception, $n(\%)$		
Yes	180 (68.18)	186 (69.66)
No	84 (31.82)	81 (30.34)
Type of contraception use, $n(\%)$		
Intrauterine device (IUD)	10 (5.55)	18 (9.68)
1-month injection	18 (10.00)	15 (8.06)
3-month injection	73 (40.56)	73 (39.25)
Pill	21 (11.67)	25 (13.44)
Condom	32 (17.78)	28 (15.05)
Implant	13 (7.22)	11 (5.91)
Others	13 (7.22)	16 (8.61)
Length of contraception use, months, median (min-max)	6 (0-99)	6 (0-99)
Reasons to stop using contraception, $n(\%)$		
Side effect	15 (8.33)	23 (12.37)
Health reason	3 (1.67)	7 (3.76)
Pregnancy planning	20 (11.11)	21 (11.29)
Expensive cost	18 (10.00)	18 (9.68)
Expired	34 (18.89)	40 (21.50)
Failure	2 (1.11)	1 (0.54)
Others (including postpartum and calendar contraception)	88 (48.89)	76 (40.86)

Table 1. Continued.

Characteristics	Implant types	
	Sinoplant, n=264	Indoplant, n=267
Menstrual pattern		
Menarche onset, years, median (min-max)	13 (10-17)	13 (10-17)
Menstrual cycle length, days, median (min-max)	28 (21-50)	28 (14-32)
Menstrual duration, days, median (min-max)	7 (3-4)	7 (3-10)
The number of pads on the day of the heaviest menstruation, median (min-max)	3 (1-7)	3 (1-9)
Ever bleeding too much or > 7 days, n(%)		
Yes	15 (5.68)	19 (7.12)
No	249 (94.32)	248 (92.88)
Bleeding between 2 menstrual periods, n(%)		
Yes	7 (2.65)	12 (4.49)
No	257 (97.35)	255 (95.51)
Ever interval between menstruation > 35 days, n(%)		
Yes	20 (7.58)	13 (4.87)
No	244 (92.42)	254 (95.13)
Ever interval between menstruation < 7 days, n(%)		
Yes	15 (5.68)	12 (4.49)
No	249 (94.32)	255 (95.51)
Never menstruated > 3 months, n(%)		
Yes	33 (12.50)	30 (11.24)
No	231 (87.50)	237 (88.76)
Cramp pain during menstruation that interferes with activities and needs medication, n(%)		
Yes	20 (7.58)	14 (5.24)
No	244 (92.42)	253 (94.76)
Past menstrual pattern, days, n(%)		
< 8	252 (95.45)	254 (95.13)
> 8	11 (4.17)	13 (4.87)
8	1 (0.38)	0 (0.00)

Table 2. Clinical parameters after 36 months of implant insertion.

Parameters	Implant types		P value
	Sinoplant (n=256)	Indoplant (n=257)	
Body weight, kg			
Baseline	56 (34-170)	57 (34-86)	
After 36 months	60 (35-85)	60 (24-86)	0.23
Systolic blood pressure, mmHg			
Baseline	110 (80-150)	110 (90-140)	
After 36 months	110 (80-178)	110 (90-156)	0.67
Diastolic blood pressure, mmHg			
Baseline	70 (60-100)	70 (60-90)	
After 36 months	70 (30-107)	70 (60-100)	0.57

Data are expressed as median (min-max). No significant difference is observed between baseline and 36 months at each parameter, $P>0.05$.

Table 3. Health condition of participants at the 36-month follow-up.

Parameters	Implant types		P value
	Sinoplant (n=256)	Indoplant (n=257)	
Body weight, kg	58.96±8.57	59.83±9.00	0.22
Upper arm circumference, cm	27.99±3.47	28.22±3.21	0.31
Systolic blood pressure, mmHg	112.88±9.55	112.25±8.92	0.43
Diastolic blood pressure, mmHg	73.96±7.19	74.61±6.89	0.51
Number of sexual intercourse, time/week	1.89±0.67	1.79±0.67	<0.05

Data are expressed as mean±SD.

four African countries. The trial revealed a significant increase in body weight among users of progestin-containing contraceptives compared to users of non-hormonal contraceptives[6]. However, in our study, weight gain at the 12- and 18-month visits after implant placement was relatively lower. At 12 months, the median weight in the Sinoplant group was 57 kg (range: 35–90 kg), while in the

Indoplant group it was 58 kg (range: 24–81 kg). At 18 months, the median weight in the Sinoplant group was 58 kg (range: 34–83 kg), and in the Indoplant group it was 60 kg (range: 36–83 kg). Moreover, at 36 months, the median weight in the Sinoplant group was 60 kg (range: 35–85 kg) and in the Indoplant group was 60 kg (range: 24–86 kg). Notably, these figures are lower than those in

Table 4. Menstrual pattern of participants at the 36-month follow-up.

Parameters	Implant types		P value
	Sinoplant (n=256)	Indoplant (n=257)	
Have had menstruation after implant placement, n(%)			
Yes	228 (89.06)	237 (92.22)	0.22*
No	28 (10.94)	20 (7.78)	
Amount of menstruation (n=465), n(%)			
≤ 3 pads/day	152 (66.67)	162 (68.35)	0.48*
> 3 pads/day	76 (33.33)	75 (31.65)	
Experiencing bleeding outside of menstruation period, n(%)			
Yes	3 (1.17)	3 (1.17)	>0.99**
No	253 (98.83)	254 (98.83)	
Length of bleeding outside of menstruation period (n=6), days, median (min-max)	0 (0-10)	0 (0-5)	>0.99***
The amount of bleeding outside of menstruation period (n=6), pad/day, median (min-max)	0 (0-21)	0 (0-2)	0.80***

*Chi square test, **Fisher's test, and ***Mann-Whitney test are used.

Table 5. Pregnancy occurrence at the 36-month follow-up.

Parameters	Implant types		P value
	Sinoplant (n=256)	Indoplant (n=257)	
Pregnancy test laboratory results, n(%)			
Positive	0 (0.00)	0 (0.00)	---
Negative	256 (100.00)	257 (100.00)	

---: no statistics are computed because observed parameter is constant.

Table 6. Post implant insertion complaints.

Parameters	Implant types		P value
	Sinoplant (n=256)	Indoplant (n=257)	
Experiencing complaints			
Yes	85 (33.20)	83 (32.30)	0.83*
No	171 (66.80)	174 (67.70)	
Dizziness/headache			
Yes	6 (2.34)	9 (3.50)	0.44*
No	250 (97.66)	248 (96.50)	
Nauseous vomit			
Yes	2 (0.78)	0 (0.00)	0.25**
No	254 (99.22)	257 (100.00)	
Spots on the face/acne			
Yes	3 (1.17)	3 (1.17)	>0.99**
No	253 (98.83)	254 (98.83)	
Weight change			
Yes	62 (24.22)	57 (22.18)	0.58*
No	194 (75.78)	200 (77.82)	
Decreased sexual desire			
Yes	2 (0.78)	4 (1.56)	0.69**
No	254 (99.22)	253 (98.44)	
Changes in menstrual patterns			
Yes	22 (8.60)	25 (9.73)	0.66*
No	234 (91.40)	232 (90.27)	
Spotting			
Yes	6 (2.34)	2 (0.78)	0.18**
No	250 (97.66)	255 (99.22)	
Impaired vision			
Yes	1 (0.40)	0 (0.00)	0.50**
No	255 (99.60)	257 (100.00)	
Others			
Yes	2 (0.78)	7 (2.72)	0.18**
No	254 (99.22)	250 (97.28)	

*Chi square test and **Fisher's test are used. Data are expressed as n(%).

previous studies, where levonorgestrel implant users reported a significant weight gain of 2.9 kg after 36 months of use[7]. However, a 2016 study reported that levonorgestrel implants do not directly cause weight gain in the short term[8]. Based on these findings, levonorgestrel implants may contribute to increased body weight. This aligns with our observations when baseline body weight of each treatment group is considered.

Aligned with the present study's findings, menstrual pattern changes are commonly reported by users of hormonal contraceptives. Combined hormonal contraceptives containing both estrogen and progesterone tend to provide more control over the menstrual cycle than progestin-only methods. However, Jadelle (a two-rod levonorgestrel implant) does not contain estrogen, resulting in frequent complaints of altered menstrual patterns. These changes often manifest as irregular menstruation, prolonged or intermittent spotting, heavy bleeding, intermenstrual bleeding or spotting, amenorrhea lasting several months, or combinations of these symptoms[9].

A systematic review comparing levonorgestrel implants and depot medroxyprogesterone acetate (DMPA) found that levonorgestrel implant users experienced a higher average number of bleeding or spotting days, but these averages remained within natural variation[10]. Another study reported that 88% of etonogestrel implant users experienced some form of menstrual abnormality, with irregular intervals being the most common[11]. Despite these side effects, no significant differences in serious adverse events were noted between different implant brands.

Studies examining the impact of contraception on female sexual function reported that women using hormonal contraceptive methods experienced reduced sexual activity, arousal, pleasure, and orgasm, as well as more difficulty with lubrication, and were more likely to report a lack of interest in sex[9,12]. However, contrasting findings have been reported in other studies. A systematic review of 36 studies involving 13 000 women found no significant differences in sexual desire among users of combined oral hormonal contraceptives[13]. Similarly, studies comparing the levonorgestrel-IUD and copper IUD reported no differences in overall sexual function or in psychological domains[14]. Additionally, a study on long-acting reversible contraceptives found no association with sexual satisfaction scores. These findings suggest that while hormonal contraception may influence women's sexual function in some cases, other studies do not indicate a clear relationship[15]. Therefore, further research is necessary to clarify the effects of contraceptives on women's sexual function.

The high acceptability of levonorgestrel implants is reflected in their continuation rates. In Argentina, a retrospective cohort study found an 86% continuation rate at one year among adolescents and young women[16,17]. Similarly, the Contraceptive CHOICE Project in the United States reported a one-year continuation rate of 83% for etonogestrel implants[18]. These findings suggest that, despite side effects, levonorgestrel implants are generally well tolerated and widely accepted by users.

This study primarily focused on clinical performance outcomes and did not directly measure levonorgestrel serum levels. As a result, we were unable to assess potential variations in hormone release or

bioavailability between Sinoplant and Indoplant, which might have provided further insights into their efficacy and side effect profiles.

Another procedure in this research that represents both a potential strength and a limitation is the IVA examination. We conducted IVA screening as part of the inclusion process to establish baseline data, confirming that no precancerous lesions were present at the start of the research and ensuring that any future lesions would not be correlated with implant use. Although hormonal implants releasing levonorgestrel have not been definitively linked to an increased risk of cervical cancer, regular screening remains essential, particularly in Indonesia, where coverage is significantly below national and international targets. As of 2023, only 7.02% of women aged 30–50 years had undergone screening using the Visual Inspection with IVA method, far below the 70% target set by the Ministry of Health. This gap contributes to a high incidence of cervical cancer, which ranks as the second most common cancer among Indonesian women, with 36 633 new cases and 21 003 deaths reported in 2021. Thus, by including IVA examinations, this study contributes to strengthening cervical cancer screening in Indonesia. However, we also recognize this as a limitation, as many women are not comfortable with vaginal procedure, one of the many underlying reasons they choose implants over other contraception methods.

Recruitment also posed a challenge due to Indonesia's vast geographical landscape. Although we conducted this study at three centers, these sites may not fully represent the diverse population and healthcare settings across Indonesia. Future studies should include broader geographic coverage and larger sample sizes to improve generalizability.

In conclusion, we found no significant differences in contraceptive effectiveness, safety, acceptability, or confounding factors between Sinoplant and Indoplant, as evaluated through quantitative analysis of pregnancy-related clinical parameters. These findings provide additional options for family planning and help reduce unmet contraceptive needs in Indonesia.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Authors' contributions

All authors contributed to the study's conceptualization. Djaswadi Dasuki, Hendy Hendarto, Delfi Lutan, Muhammad N. Rahman, Sarrah Ayuandari, Endah Rahmawati, Adi Ariffianto, and Irfan Haris were involved in the investigation. The study was designed by Muhammad N. Rahman, Muhammad O. Prabudi, Indra G. Munthe, Jimmy Y. Annas, Shinta Prawitasari, Muhammad Lutfi, Arif Tunjungseto, Sarrah Ayuandari, Adi Ariffianto, and Irfan Haris. The manuscript was written by Djaswadi Dasuki, Muhammad N. Rahman, Sarrah Ayuandari, Endah Rahmawati, and Adi Ariffianto.

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