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A 1-year comparison of TCu380Ag versus TCu380A intrauterine contraceptive devices in India

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Abstract

Objective: To compare TCu380Ag and TCu380A intrauterine contraceptive devices after 1 year of use.

Methods: A prospective randomized controlled trial was conducted among healthy married women aged 20–35 years who attended the family planning clinics of three tertiary centers in India between August 1, 2015, to March 31, 2018. The TCu380Ag group (n=300) received one of three sizes of this device depending on uterocervical length: maxi (8.0–9.0 cm), normal (7.0–8.5 cm), or mini (6.0–7.5 cm). The remaining 300 participants received TCu380A. Follow-up was conducted at 3-monthly intervals to assess continuation rate, acceptability, efficacy, adverse effects, and complications.

Results: The TCu380Ag group had a higher continuation rate than the TCu380A group at 1 year (84.0% vs 75.8%; *P*=0.01), with an efficacy of 99.6% versus 100.0% (*P*>0.05). Overall estimated continuation rates were 94.5% (95% confidence interval [CI] 91.7%–96.4%) and 88.4% (95% CI 83.2%–91.5%), respectively (*P*=0.026). Use of TCu380Ag was associated with fewer adverse effects (heavy menstrual bleeding, abdominal pain, or expulsion) when compared with TCu380A (*P*>0.05 for all comparisons). Discontinuation rates owing to adverse effects were 6.59% for TCu380Ag versus 13.26% for TCu380A (*P*=0.01).

Conclusions: Varying sizes of TCu380Ag could provide an alternative to TCu380A.

KEYWORDS

Acceptability; Continuation rate; Efficacy; Intrauterine contraceptive device; TCu380A; TCu380Ag

1 | INTRODUCTION

An intrauterine contraceptive device (IUCD) is the ideal method for women who require long-term reversible contraception as this approach offers high efficacy (99.8%), low expulsion rate (2.4%), and long lifespan (10 years).[1] Nonetheless, IUCDs are associated with adverse effects, including increased menstrual flow and dysmenorrhoea, which are barriers for some potential users. Continuation of IUCD use at 12 months is suboptimal owing to adverse effects and inadequate health information provided at time of insertion.[2] Continuation rates could be improved if the adverse effects of IUCDs were minimized.

In the Nova-T IUCDs, both 200 and 380 (Bayer (Pty) Ltd, Isando, South Africa), silver (Ag) is added to stabilize the copper (Cu) wire, thereby decreasing its fragmentation with extended use and so prolonging the lifespan of this device.[3] A 3-year study found that Nova-T had substantially greater efficacy than an IUCD that lacked Ag (CuT200).[3] TCu380Ag offers a 5-year lifespan and is available in three different sizes, with sterile disposable uterine sonography provided separately for measurement of uterine size.[4] Consequently, it was hypothesized that use of TCu380Ag might overcome adverse effects, while improving acceptability and sustainability.

The aim of the present study was to compare TCu380Ag and TCu380A among a group of Indian women requiring long-term reversible contraception.

2 | MATERIALS AND METHODS

A prospective randomized controlled trial was conducted in the family planning outpatient departments of three tertiary centers in India between August 1, 2015, and March 31, 2018. The present study sites were: the All India Institute of Medical Sciences (New Delhi), the Calcutta National Medical College and Hospital (Kolkata), and the Prathima Institute of Medical Sciences (Karimnagar). The protocol was approved by the ethics committee at each of the three sites and registered in the Clinical Trials Registry - India as 2015/07/009325. Audio visual and written informed consent was obtained from the participants at the time of screening.

As there was no similar prospective parallel comparative study of the two IUCDs, the sample size with prior power could not be calculated; therefore, the present study was conducted in pilot mode.

Women who expressed a need for an IUCD were screened as potential participants immediately after medical termination of pregnancy (MTP); in the prenatal period for postpartum insertion; or for interval insertions (between 5 and 8 days of menses). The women were advised to attend follow-up visits at 1, 3, 6, 9, and 12 months after insertion of the IUCD. Women with contraindications to IUCD insertion were excluded from the present study.

A total of 600 healthy married women, aged 20–35 years and with at least one live child, were recruited after screening. Each site enrolled 100 women in the TCu380A group and 100 women in the TCu380Ag group, giving a total of 300 women per group. The TCu380Ag group was also subdivided by size of the device used: maxi (8.0–9.0 cm), normal (7.0–8.5 cm), or mini (6.0–7.5 cm), depending on the uterocervical length. All participants underwent a general, physical, and vaginal examination. In addition, clinical, menstrual, obstetric, and contraceptive histories were taken.

Each site was provided with 200 sealed and numbered opaque envelopes that contained the group allocation code generated by computer randomization. Participants were allocated to a group by opening an envelope and stating the code.

Following measurement of uterine size by uterine sound, the IUCDs were inserted under aseptic conditions using the no touch technique. The vertical arm length of TCu380A is 36.0 mm, whereas for TCu380Ag this measure is 38.0 mm (maxi), 33.0 mm (normal), or 30.5 mm (mini). The size of TCu380Ag inserted was as per uterine size for interval insertions but as per the gynecologist's opinion for MTP and postpartum insertions.

The time taken for IUCD insertion was defined as the time between the start of uterine sound and cutting the IUCD thread. Pain during IUCD insertion was recorded using a numerical rating scale that ranged from zero (no pain) to 10 (worst pain). The time taken and pain during IUCD insertion were recorded in two centres.

Participants were given a menstrual diary card to record days of bleeding. Menstrual cycle and complaints were recorded at each follow-up visit. A speculum and/or vaginal examination was performed to see the thread. Normal menstrual cycle was defined as a duration of 28–30 days, with 5–7 days of bleeding (60–80 mL/day). Amenorrhea was defined as no menstruation for greater than 3 months. Heavy menstrual bleeding (HMB) was defined as bleeding for greater than 7 days and as per the woman's perception.

The primary objective was assessment of continuation rate, acceptability, efficacy, and adverse effects at 1 year of IUCD use. The secondary objective was to compare the complication rates between the two groups. The continuation rate was defined as the percentage of women using the IUCDs at 1 year. The efficacy rate was calculated as the number of nonpregnant IUCD users/total number of IUCD users × 100.

The data were recorded using an Excel spreadsheet (Microsoft, Redmond, WA, USA) and analyzed using SPSS version 22.0 (IBM, Armonk, NY, USA). Continuous variables were tested for normality assumptions using the Kolmogorov–Smirnov test. The normally distributed variables were expressed as descriptive statistics, including mean, standard deviation, and range. Categorical data were presented as frequency and percentage. Comparisons of frequency data across categories were performed using the χ^2 or Fisher exact test, as appropriate. The Mantel-Haenszel χ^2 test was conducted to control for a clustering effect. Mean values of continuous variables meeting normality assumption and median values of non-normal data were compared using an independent *t* test and non-parametric Mann-Whitney *U* test, respectively. Kaplan-Meier survival analysis was performed to estimate the overall continuation rate, with the 95% confidence interval (CI). Comparison of continuation rates was tested using a log-rank test. A two-tailed *P* value of less than 0.05 was considered statistically significant.

3 | RESULTS

Allocation of the participants at enrollment, follow-up, and analysis is outlined in Figure 1.

Of the 600 participants, 304 (50.7%) were aged 25–30 years; 151 (25.1%) were aged 30–32; and 145 (24.2%) were aged 32–35 years. The mean parity was 2.58 (range 1–5). Parity in the TCu380Ag and TCu380A groups was 2.54 ± 1.04 and 2.6 ± 1.14, respectively (*P*=0.56). The mean number of live children was 1.97, with values of 1.91 ± 0.82 and 1.83 ± 0.63 in the TCu380Ag and TCu380A groups, respectively (*P*=0.08). The mean number of induced abortions was 0.7 (range 1–3), with values of 0.63 ± 0.64 and 0.80 ± 0.91 in the TCu380Ag and TCu380A groups, respectively (*P*=0.14). In all, 333 (55.5%) women had two live children; 183 (30.5%) had one live child; 63 (10.5%) had three live children; and 23 (3.5%) had four live children.

The sociodemographic characteristics are shown in Table 1. Statistically significant between-group differences were found for educational level (*P*=0.001), residence (*P*=0.007), and religion (*P*=0.043).

Table 2 depicts the type of IUCD insertion for each group. There was no difference in number of interval, postpartum and post-MTP insertions between the two groups (*P*>0.05).

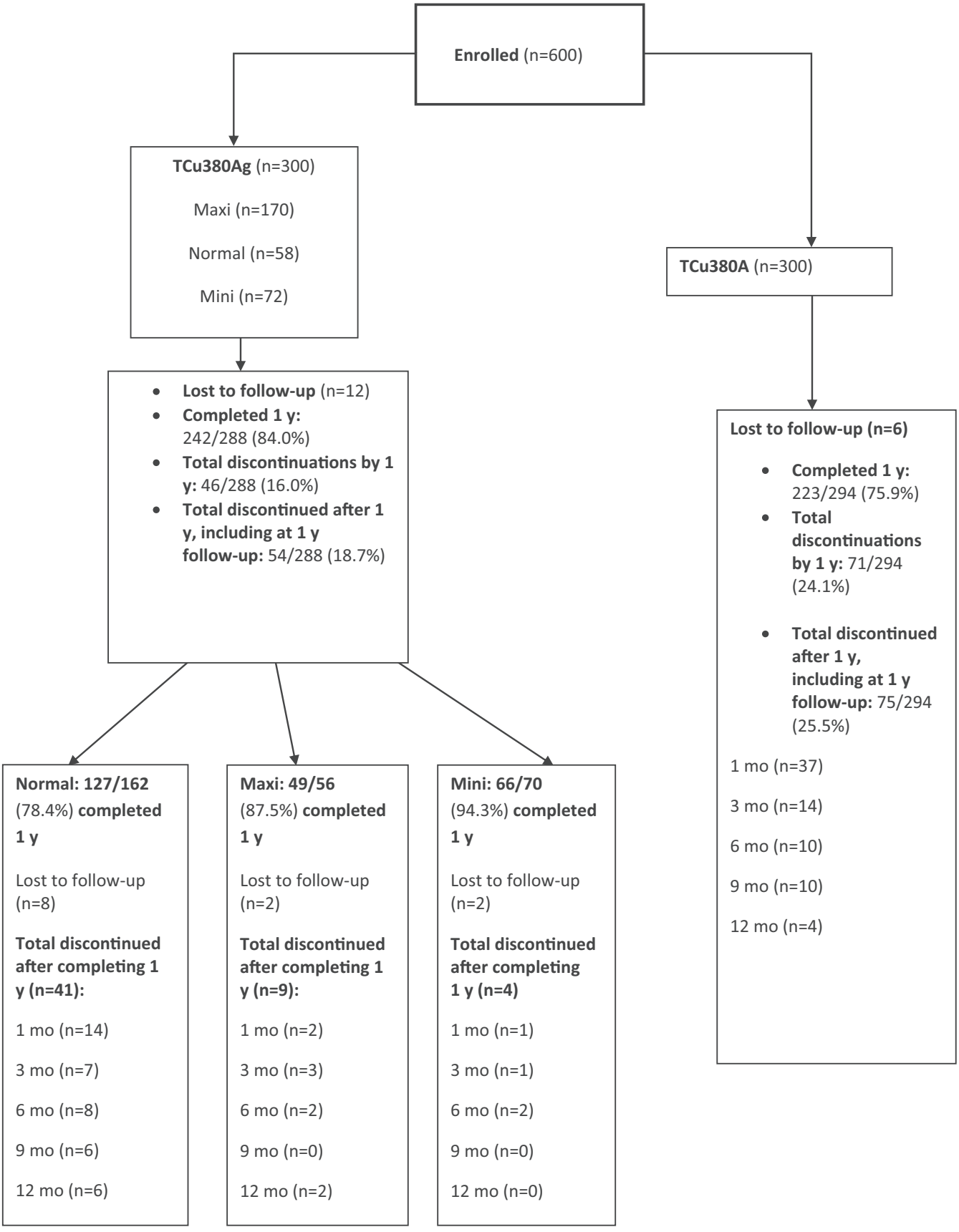

FIGURE 1 Study flow chart. Participants allocated to the TCu380Ag group received one of three sizes of this device depending on uterocervical length: maxi (8.0–9.0 cm), normal (7.0–8.5 cm), and mini (6.0–7.5 cm).

TABLE 1 Sociodemographic characteristics of the participants.[a]

Characteristic	TCu380Ag group (n=300)[b]				TCu380A group (n=300)	*P* value[c]	Total cohort (n=600)
	Normal (n=170)	Maxi (n=58)	Mini (72)	Total (n=300)			
Residence							
Rural	13 (7.7)	3 (5.2)	0 (0.0)	16 (5.3)	36 (12.0)	0.007	52 (8.7)
Urban slum	16 (9.4)	19 (32.7)	0 (0.0)	35 (11.7)	42 (14.0)		77 (12.8)
Urban	141 (82.9)	36 (62.1)	72 (100.0)	249 (83.0)	222 (74.0)		471 (78.5)
Educational level							
Illiterate or can read and write	17 (10.0)	8 (13.8)	5 (6.9)	30 (10.0)	30 (10.0)	0.001	60 (10.0)
Up to middle school (8 years of formal education)	65 (38.2)	23 (39.7)	62 (86.1)	150 (50.0)	87 (29.0)		237 (39.5)
Secondary and above	88 (51.8)	27 (46.5)	5 (6.9)	120 (40.0)	183 (61.0)		303 (50.5)
Occupation							
Unskilled or skilled worker	18 (10.6)	12 (20.7)	10 (13.9)	40 (13.0)	45 (15.0)	0.443	85 (14.2)
Clerical or professional	25 (14.7)	12 (20.7)	5 (6.9)	42 (14.0)	51 (17.0)		93 (15.5)
Housewife	127 (74.7)	34 (58.6)	57 (79.2)	218 (73.0)	204 (68.0)		422 (70.3)
Religion							
Hindu or Sikh	158 (92.9)	49 (84.5)	62 (86.1)	269 (89.7)	258 (86.0)	0.043	527 (87.9)
Muslim	9 (5.3)	6 (10.3)	5 (6.9)	20 (6.7)	36 (12.0)		56 (9.3)
Christian	3 (1.8)	3 (5.2)	5 (6.9)	11 (3.6)	6 (2.0)		17 (2.8)
Type of family							
Joint	84 (49.4)	22 (37.9)	15 (20.8)	121 (40.3)	141 (47.0)	0.100	262 (43.7)
Nuclear	86 (50.6)	36 (62.1)	57 (79.2)	179 (59.7)	159 (53.0)		338 (56.3)
Monthly income, Indian rupees							
5000–20 000	101 (59.4)	30 (51.7)	50 (69.4)	181 (60.3)	177 (59.0)	0.922	358 (59.7)
20 001–50 000	39 (22.9)	19 (32.8)	22 (30.6)	80 (26.7)	81 (27.0)		161 (26.8)
≥50 001	30 (17.7)	9 (15.5)	0 (0.0)	39 (13.0)	42 (14.0)		81 (13.5)

[a]Values are given as number (percentage), unless indicated otherwise.
[b]Participants allocated to the TCu380Ag group received one of three sizes of this device depending on uterocervical length: maxi (8.0–9.0 cm), normal (7.0–8.5 cm), and mini (6.0–7.5 cm).
[c]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.

Outcomes during IUCD insertion were assessed among 200 women per group (Table 3). The pain score at the time of insertion was lower in the TCu380Ag group than in the TCu380A group (score of 0–5; $P<0.001$). Time taken to insert the IUCD was also lower in the TCu380Ag group than in the TCu380A group (0–1 minute; $P=0.020$).

TABLE 2 Type of intrauterine contraceptive device insertion.[a]

Group	Type of insertion		
	Interval	Post-MTP	Postpartum
TCu380Ag (n=300)	94 (31.3)	91 (30.3)	115 (38.3)
TCu380A (n=300)	89 (29.7)	84 (28.0)	127 (42.3)
P value[b]	0.660	0.530	0.318
Total cohort (n=600)	183 (30.5)	175 (29.1)	242 (40.3)

Abbreviation: MTP, medical termination of pregnancy.
[a]Values are given as number (percentage), unless indicated otherwise.
[b]Based on Chi-square test; cut-off value for significance is $P<0.05$.

As seen in Table 1, statistically significant between-group differences were found for residence, educational level, and religion. To control for a clustering effect on continuation rate, the Mantel-Haenszel χ^2 test was performed at 1 year. The corrected value was 3.46 ($P=0.063$). After adjusting for type of IUD insertion, the continuation rate remained statistically significant ($P=0.048$). Since the cluster-adjusted continuation rate was statistically insignificant, all further analyses were conducted by pooling the group data.

The continuation rate over time is shown in Table 4. The continuation rates at 12 months were 84.0% and 75.8% in the TCu380Ag and TCu380A groups, respectively. The discontinuation rates at 1–3, 3–6, 6–9, 9–12 and at 12 months were less in TCu380Ag ($P<0.05$). As shown in Figure 2, the overall continuation rates for the TCu380Ag and TCu380A groups were 94% (95% CI 91%–96%) and 88% (95% CI 83%–91%), respectively ($P=0.026$). The discontinuation rates by time

TABLE 3 Outcomes during intrauterine contraceptive device insertion.[a]

Outcome	CuT380Ag (n=200)	CuT380A (n=200)	*P* value[b]	Total cohort (n=400)
Pain score at time of insertion				
0–1	53 (26.5)	11 (5.5)	0.001	64 (16.0)
2–5	118 (59.0)	150 (75.0)	0.001	268 (67.0)
6–8	25 (12.5)	29 (14.5)	0.558	54 (13.5)
9–10	4 (2.0)	10 (5.0)	0.172	14 (3.5)
Time taken for insertion, min				
0–1	46 (23.0)	28 (14.0)	0.020	74 (18.5)
1–2	98 (49.0)	102 (51.0)	0.689	200 (50.0)
2–3	32 (16.0)	44 (22.0)	0.126	76 (19.0)
3–4	24 (12.0)	26 (13.0)	0.762	50 (12.5)

[a]Values are given as number (percentage), unless indicated otherwise.
[b]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.

depicted in Figure 3 indicate that the discontinuation rate was highest during the first month following insertion for both IUCDs.

Given the data shown in Table 4, Figures 2 and 3, a post hoc power calculation was conducted. The power was 66%, which confirmed that the present study was a pilot study.

Table 5 shows the reasons for discontinuation of the IUCDs. The TCu380Ag group experienced fewer contraceptive-related adverse effects than did the TCu380A group (P=0.007). HMB and spontaneous expulsion as reasons for discontinuation were significantly less frequent in the TCu380Ag group.

One pregnancy following partial expulsion was observed in the TCu380Ag group (maxi size, interval insertion) at 6 months of follow up. This participant had a history of missed periods; bulky uterus; positive urine pregnancy test; a 5-week intrauterine pregnancy by ultrasonography; and experience of partial expulsion following TCu insertion on two previous occasions. She opted to undergo MTP followed by reinsertion of the IUCD.

Discontinuations related to the type of insertion are outlined in Table 6. In the TCu380Ag group, for interval insertions where different sizes were used as per uterine size, discontinuations were significantly less frequent.

Where history was taken in full by the investigators, adverse effects were recorded among only 188 women in the TCu380Ag group and 194 in the TCu380A group, whereas Table 5 depicts the reasons for discontinuation in all women who completed the study. Abdominal pain (34 [17.5%] vs 18 [9.6%]) (P=0.02) and husband feeling thread/burning (0 [0.0%] vs 4 [2.1%]) (P=0.05) were greater in the TCu380A group than in the TCu380Ag group. Adverse effects such as HMB {68 (23.1%) versus 50 (17.5%)}, intermenstrual bleeding {22 (7.2%) versus 12 (4.2%)}, postcoital bleeding {(04 (1.5%) versus 03 (1.1%)},

TABLE 4 Continuation of intrauterine contraceptive device use over time.[a]

	Month				
Measure	**1**	**3**	**6**	**9**	**12**
TCu380Ag monitored	300 (LFU=0)	298 (LFU=2)	294 (LFU=6)	288 (LFU=12)	288 (LFU=12)
TCu380Ag continuation*	297/300 (99.0)	281/298 (94.3)	266/294 (90.4)	248/288 (86.1)	242/288 (84.0)
TCu380A monitored	298 (LFU=2)	298 (LFU=2)	296 (LFU=4)	294 (LFU=6)	294 (LFU=6)
TCu380A continuation*	287/298 (96.3)	261/298 (87.6)	245/296 (82.8)	233/294 (79.2)	223/294 (75.8)
P value[b,*]	0.026	0.004	0.005	0.029	0.014
Discontinuations at time interval	**1–3 m**	**3–6 m**	**6–9 m**	**9–12 m**	**>12 m**
TCu380Ag **discontinued	17/298 (5.7)	28/298 (9.4)	40/294 (13.6)	46/288 (15.9)	54/288 (18.7)
TCu380A **discontinued	37/298 (12.4)	51/298 (17.1)	61/296 (20.6)	71/294 (24.1)	75/294 (25.5)
P value[b,**]	0.004	0.004	0.024	0.014	0.050
Total continued	584/598 (97.6)	542/596 (90.9)	511/590 (86.6)	481/582 (82.6)	467/582 (80.2)

Abbreviation: LFU, lost to follow-up.
[a]Values are given as number (percentage), unless indicated otherwise.
[b]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.
*P value test between TCu380Ag continuation and TCu380A continuation.
**P value test between TCu380Ag **discontinued and TCu380A **discontinued.

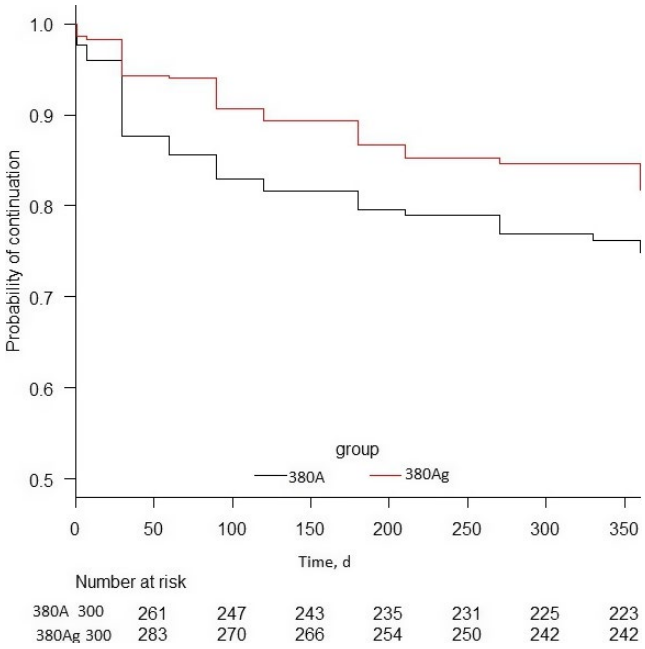

FIGURE 2 Kaplan-Meier survival analysis of continuation rate among the TCu380Ag (380Ag) and TCu380A (380A) groups.

vaginitis {91 (30.9%) versus 89 (30.8%)}, urinary tract infections {8 (2.6%) versus 06 (2.1%)}, and backache {17 (5.7%) versus 11 (3.7%)} were greater in the TCu380A group than in the TCu380Ag group (P>0.05). Dysmenorrhea {08 (2.7%) versus 06 (2.1%)}, pelvic inflammatory disease {08 (2.7%) versus 07 (2.4%)}, dyspareunia {01 (0.3%) versus 02 (0.7%)}, thread not felt {09 (3.2%) versus 06 (2.1%)} were similar in the two groups.

Menstrual cycles were observed among 285 and 283 women in the TCu380Ag and TCu380A groups, respectively. Regular menstrual cycles and the mean number of days of bleeding after IUCD

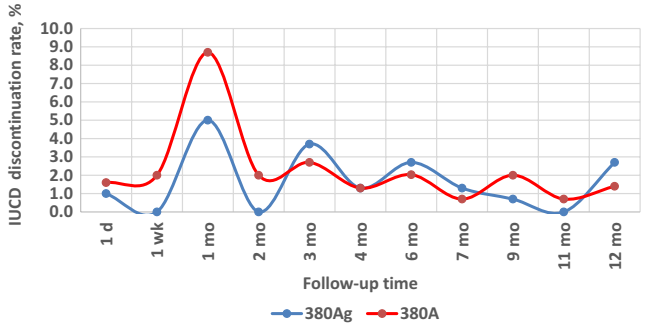

FIGURE 3 Intrauterine contraceptive device (IUCD) discontinuation rate by time for the TCu380Ag (CuTAg); n=54) and TCu380A (CuTA; n=75) groups.

Insertion were 259 (90.8%) versus 235 (83.0%) and 4.84 ± 1.656 versus 5.3 ± 2.428 in the TCu380Ag and TCu380A groups, respectively (P=0.005 and P=0.01). In the TCu380Ag group versus the TCu380A group, bleeding more than the usual flow was reduced (48 [16.8%] vs 99 [34.9%]; P<0.05), as was prolonged bleeding (52 [18.2%] vs 69 [24.4%]; P>0.05). No ectopic pregnancy or misplaced IUCD was found for either group after 1 year.

Comparison of the three sizes of TCu380Ag is shown in Table 7. No difference was found in sociodemographic profile and continuation rates by type of insertion (P>0.05). Episodes of HMB was seen more often with the maxi size (n=18, 32.2%) versus the mini (n=11, 15.7%) and normal (n=21, 13.0%) sizes (P=0.004). Other adverse effects, regular menstrual cycles, change in mean number of days of bleeding, complaints of prolonged and excessive bleeding were similar for the three sizes of TCu380Ag (P>0.05).

4 | DISCUSSION

The continuation rates of TCu380Ag compared with TCu380A were higher at 1 year (84.0% versus 75.8%) and after 1 year (81.3% versus 74.5%) (P<0.05). HMB and spontaneous expulsions as reasons for discontinuations were less frequent with TCu380Ag. The present study found that most of the IUCD users were Hindu housewives aged younger than 30 years, who were educated to at least secondary level and had at least two live children. They tended to reside in an urban area, as a complete family unit, with a monthly family income of less than 20 000 Indian rupees. This sociodemographic profile was in line with a previous Indian study of IUCD use.[5]

Women who received TCu380Ag in the present study reported less pain during IUCD insertion than did women in the TCu380A group. This finding might reflect differences in size, packaging, and loading technique for TCu380Ag, which in turn could reduce insertion time. This finding is important as women often refrain from choosing IUCDs because they anticipate pain at insertion.[6]

The 1-year continuation rate of 79.9% in the present study was comparable to previously reported rates of 76.0% [7] and 88.3%.[4] The current continuation rate for IUCD use was higher than the rates of 58 and 68% for oral contraceptive pills and injectable contraceptives, respectively.[7,8] Of note, continuation rates with TCu380Ag were higher than those with TCu380A at all time points assessed despite similar counseling and follow-up between the two groups. The between-group differences were statistically significant for interval insertions but not for postpartum or MTP insertions. This difference could be because TCu380Ag insertions were made as per the uterocervical length for interval insertions. The 12-month continuation rate for TCu380Ag (84.0%) was comparable to the rate reported for Nova-T380A (88.3%).[4]

The present study demonstrated that the 1-year continuation rate for postpartum insertions (82.2%) was greater than that for interval (78.1%) and MTP (71.3%) insertions in both groups. Previous studies reported a higher 6-month continuation rate for postpartum insertions (88.2%) versus interval insertions (81.8%).[9–12] Postpartum insertions

TABLE 5 Reasons for discontinuation of intrauterine contraceptive device.[a]

Reason	TCu380Ag (n=288)	TCu380A (n=294)	*P* value[b]	Total cohort (n=582)
Adverse effects related to IUCD	19 (6.6)	39 (13.3)	0.007	58 (9.9)
Heavy menstrual bleeding	6 (2.1)	16 (5.4)	0.034	22 (3.7)
Heavy menstrual bleeding + dysmenorrhea	5 (1.7)	13 (4.4)	0.061	18 (3.1)
Intermenstrual bleeding	2 (0.7)	2 (0.7)	0.990	4 (0.7)
Abdominal pain	2 (0.7)	6 (2.0)	0.286	8 (1.4)
Pelvic inflammatory disease	4 (1.4)	2 (0.7)	0.446	6 (1.0)
Adverse effects not related to IUCD	4 (1.4)	0 (0.0)	0.059	4 (0.7)
Weight gain or swelling feet	4 (1.4)	0 (0.0)	0.059	4 (0.7)
Medically indicated	6 (2.1)	6 (2.0)	0.971	12 (2.1)
Developed a medical disease	2 (0.7)	4 (1.4)	0.686	6 (1.0)
Incomplete abortion	4 (1.4)	2 (0.7)	0.446	6 (1.0)
Personal reasons	8 (2.8)	5 (1.7)	0.414	13 (2.2)
Personal choice	4 (1.4)	1 (0.3)	0.212	5 (0.8)
Divorced	2 (0.7)	2 (0.7)	0.990	4 (0.7)
Planning a pregnancy	2 (0.7)	2 (0.7)	0.990	4 (0.7)
Technique related	17 (5.9)	25 (8.5)	0.225	42 (7.2)
Spontaneous expulsion	7 (2.4)	19 (6.4)	0.019	26 (4.5)
Partial expulsion	2 (0.7)	0 (0.0)	0.244	2 (0.3)
Partial expulsion and pregnancy	1 (0.3)	0 (0.0)	0.495	1 (0.2)
Thread not seen	7 (2.4)	6 (2.0)	0.750	13 (2.2)
Discontinuation rate due to at least one reason	54 (18.8)	75 (25.4)	0.050	129 (22.2)

Abbreviation: IUCD, intrauterine contraceptive device.
[a]Values are given as number (percentage), unless indicated otherwise.
[b]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.

are therefore acceptable despite the expulsion rate (6.0%). In the present study, continuation rates following MTP insertions in both groups were lower than for the other types of insertion even though contraceptive adverse effects were similar to those reported for interval insertions. This may be because once fear of MTP has passed, women get IUCDs removed because they fear complications, hence counseling is essential at the time of insertion.

The IUCDs used in the present study showed 99.8% effectiveness, with 99.6% and 100.0% for TCu380Ag and TCu380A users, respectively. Pregnancy following partial expulsion of TCu380Ag was observed in one case; however, the affected woman had history of IUCD expulsions. The uterine factor could underpin IUCD expulsions, with an appreciable relationship reported between expulsions and contraceptive failure.[13,14] The current failure rate with TCu380Ag (0.34%) was less than the reported overall cumulative accidental pregnancy rate of 0.8% and 0.5% at 1 year of using Nova-T380.[4,15] A 12-year study of Nova-T200 reported an overall cumulative accidental pregnancy rate of 3.5%,[16] whereas Nygren et al.[3] reported Nova-T to be superior to CuT200 for preventing unwanted pregnancy.

Contraceptive adverse effects were the most common reasons for discontinuation in the present study (9.9%), followed by technique-related reasons (e.g. expulsions or thread; 7.2%). Episodes of HMB with or without dysmenorrhoea are reported as the most common reason for discontinuation of TCu380A.[4,17,18] Of note, this reason for discontinuation was given less often for TCu380Ag than for TCu380A in the present study. The 3.8% discontinuation rate due to HMB at 12 months for the TCu380Ag group was comparable to 4.4% cumulative 1-year discontinuation rate due to bleeding in the Nova-T380 study.[4] Nonsteroidal anti-inflammatory drugs and/or tranexamic acid are recommended as the first and/or second line of therapy if bleeding and pain are associated with IUCD use.[17,18]

Other contraceptive adverse events as reasons for discontinuation (e.g. pelvic inflammatory disease, irregular periods, and abdominal pain) showed no statistically significant between-group differences in the present study. Overall, bleeding and pain as the reason for discontinuation were less frequent in the TCu380Ag group than in the TCu380A group. The current rate of 9.9% for discontinuations due to IUCD adverse effects was less than that reported in a Bangladeshi study (47.3%).[9]

The overall discontinuation rate following expulsions in the present study (5.0%) was less than the previously reported rate (13.0%).[4,10] The expulsion rate of 3.4% with TCu380Ag was also less than the 4.9% and 5.6% rates recorded for Nova-T200 and Nova-T380, respectively. The 5-year clinical experience with Nova-T380 found an expulsion rate of 1.3%.[4,15,16]

Continuation rates are known to improve if women are counseled that 'thread not seen' is not a valid reason for discontinuation and that immediate reinsertion can be performed after expulsions. The rate of women who discontinued as they wished to become pregnant was

TABLE 6 Discontinuations related to device as per type of insertion.[a]

Type of insertion	No. of participants enrolled	Continued after 1 year	Discontinued	Reason for discontinuation	No. of participants lost to follow-up
Interval insertion*	201	149/191 (78.0)	42/191 (22.0)	NA	10
TCu380Ag	110	88/102 (86.3)	14/102 (13.7)	Thread not seen/felt-02 Heavy bleeding-06 Pregnancy + Partial expulsion-01 Obesity-02 Wants conception-02	8
TCu380A	91	61/89 (68.5)	28/89 (31.5)	Expelled-10 Pain abdomen-06 Heavy Bleeding-08 Wants conception-02 Divorced-02	2
P value[b]		0.003			
Post MTP*	168	114/160 (71.2)	46/160 (28.2)	NA	8
TCu380Ag	85	55/81 (67.9)	26/81 (32.1)	Expelled (n=4) Incomplete abortion (n=4) Pelvic inflammatory disease (n=4) Abdominal pain (n=2) Heavy menstrual bleeding (n=2) Intermenstrual bleeding (n=2) Divorced (n=2) Kidney disease (n=2) Swelling feet (n=2) Personal choice (n=2)	4
TCu380A	83	59/79 (74.7%)	20/79 (25.3)	Incomplete abortion (n=2) Backache (n=2) Heavy menstrual bleeding (n=10) Intermenstrual bleeding (n=2) Gastritis (n=2) Developed heart problem (n=2)	4
P value[b]		0.343			
Postpartum*	231	190/231 (82.2)	41/231 (17.8)	NA	0
TCu380Ag	105	91/105 (86.7%)	14/105 (13.3)	Device expelled (n=5) Thread not seen or felt (n=5) Heavy menstrual bleeding (n=2) Personal choice (n=2)	0
TCu380A	126	99/126 (78.6)	27/126 (21.4)	Device expelled (n=8) Device partially expelled (n=1) Thread not seen or felt (n=6) Heavy menstrual bleeding (n=11) Personal choice (n=1)	0
P value[b]		0.109			
P value[c]	0.048				

Abbreviation: NA, not applicable.
[a]Values are given as number (percentage), unless indicated otherwise.
[b]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.
[c]Based on the corrected Mantel-Haenszel test.
*Difference in discontinuations in interval, post-MTP and postpartum calculated by *P* value.

0.7% in the present study (with no between-group difference). This rate was less than the rate of 57.0% previously reported.[19]

The TCu380Ag group reported fewer discontinuations following adverse events and expulsions than the TCu380A group. This difference might be explained by the silver component, the insertion technique, and the different sizes of TCu380Ag.

Maximum discontinuations 9.3% (54/582) were at 1 month as shown in Figure 3, although significantly less in TCu380Ag. High discontinuations in month one might be explained by more expulsions and medically indicated IUCD removal following incomplete abortion and postpartum hemorrhage. Healthcare providers must counsel about possible adverse effects, follow up at 1 month, and re-offer IUCD in cases of expulsion.

TABLE 7 Comparison of the different sizes of TCu380Ag.[a]

Measure	Size of TCu380Ag[b]			*P* value[c]	Total cohort
	Normal	Maxi	Mini		
Pain intensity score at IUCD insertion (200 acceptors)					
0–1	33 (26.2)	8 (19.1)	12 (37.4)	0.203	53 (26.5)
2–5	72 (57.1)	30 (71.4)	16 (50.0)	0.145	118 (59.0)
6–8	19 (15.1)	4 (9.5)	2 (6.3)	0.372	25 (12.5)
9–10	2 (1.6)	0 (0.0)	2 (6.3)	0.204	4 (2.0)
Total	126	42	32	NA	200
Time taken for IUCD insertion, min (200 users)					
0–1	20 (15.9)	15 (35.7)	11 (34.3)	0.008	46 (23.0)
1–2	64 (50.8)	22 (52.4)	12 (37.5)	0.359	98 (49.0)
2–3	22 (17.4)	3 (7.1)	7 (21.9)	0.160	32 (16.0)
3–4	20 (15.9)	2 (4.8)	2 (6.3)	0.103	24 (12.0)
Total	126	42	32	NA	200
Continuation rate					
Total	170	58	72	NA	300
1 mo	167 (98.2)	58 (100.0)	72 (100.0)	0.581	297/300 (99.0)
3 mo	155 (91.2)	55 (94.8)	71 (98.6)	0.082	281/298 (94.3)
6 mo	145 (85.3)	51 (87.9)	70 (97.2)	0.017	266/294 (90.4)
9 mo	133 (78.2)	49 (84.5)	66 (91.7)	0.038	248/288 (86.1)
12 mo	127 (74.7)	49 (84.5)	66 (91.7)	0.007	242/288 (84.0)
>12 mo	121 (71.2)	47 (81.0)	66 (91.7)	0.002	234/288 (85.4)
Discontinuation at different time intervals, mo	Continued/Monitored (%) (LFU=8)	C/M (%) (LFU=2)	C/M (%) (LFU=2)	NA	C/M (%) (LFU=0)
1–3 (LFU=2)	13/168 (7.7)	3/58 (5.2)	1/72 (1.4)	0.147	17/298 (5.7)
3–6 (LFU=4)	8/166 (4.8)	2/56 (3.6)	1/72 (1.4)	0.483	11/294 (3.7)
6–9 (LFU=6)	8/162 (4.9)	2/56 (3.6)	2/70 (2.9)	0.920	12/288 (4.2)
9–12 (LFU=0)	6/162 (3.7)	0/56 (0.0)	0/70 (0.0)	0.137	6/288 (2.1)
12 (LFU=0)	6/162 (3.7)	2/56 (3.6)	0/70 (0.0)	0.227	8/288 (2.8)
Total discontinuations	41/162 (25.3)	9/56 (16.1)	4/70 (5.7)	0.002	54/288 (18.7)

Abbreviations: LFU, lost to follow-up; IUCD, intrauterine contraceptive device; NA, not applicable.
Pain intensity score while IUCD insertion recorded in Numerical Rating Scale (0–10).
[a]Values are given as number (percentage), unless indicated otherwise.
[b]Participants allocated to the TCu380Ag group received one of three sizes of this device depending on uterocervical length: maxi (8.0–9.0 cm); normal (7.0–8.5 cm); and mini (6.0–7.5 cm).
[c]Based on Chi-square/Fisher exact test as appropriate; cut-off value for significance is $P<0.05$.

Menstrual irregularities and fear of complications are the main barriers to long-term acceptance of IUCDs.[18,20–22] Women who received TCu380Ag in the present study tended to experience fewer issues with the device than those who received TCu380A. Consequently, TCu380Ag is likely to have good acceptability. On comparing three sizes of TCu380Ag with each other, continuation rates were highest for mini, followed by maxi and normal at 12 months ($P<0.05$), although no difference was shown in adverse effects. With mini, less time was taken for insertion and pain score was lower.

Strengths of the present study included the fact that it had a multicenter design and participants could be quickly enrolled. As a randomized controlled trial, the data obtained will provide robust evidence on the acceptability of TCu380Ag.

The main limitation of the present study was the inclusion criteria, which were based on marital status, age, and number of live children; therefore, generalization of the current findings could be problematic. In addition, follow-up did not occur beyond 12 months. The adverse effects or complications of the two IUCDs should now be compared at 5 years after insertion.

In conclusion, TCu380Ag and TCu380A were equally effective at 1 year after insertion; however, TCu380Ag was associated with higher levels of continuation and acceptance than TCu380A owing to reduced adverse effects. The current findings suggest

that TCu380Ag could be offered to women who wish to space future pregnancies.

AUTHOR CONTRIBUTIONS

AK contributed to study conception and design. RS contributed to study conception and design; conducting the study; acquisition, analysis, and interpretation of the data; and writing the first draft of the manuscript. RS also agreed to be accountable for all aspects of the work by ensuring that questions related to its accuracy or integrity were appropriately investigated and resolved. HK and AV contributed to conducting the study, as well as acquisition and analysis of the data. PV contributed to acquisition, analysis, and interpretation of the data. CNP contributed to study conception and design. All authors contributed to revising the manuscript and gave final approval of the version to be published.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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