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**A COMPARATIVE STUDY OF THE
TCu 380A IUD AND THE TCu 200 IUD
IN YAOUNDE, CAMEROON**

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I. Introduction

A study comparing the Copper T 380A (TCu 380A) intrauterine device (IUD) and the Copper T 200 (TCu 200) IUD was conducted at the University of Yaoundé in Yaoundé, Cameroon. The purpose of this study was to evaluate the safety and efficacy of the TCu 380A IUD compared to the locally used TCu 200 IUD. The factors evaluated were complications and complaints, participant's status after twelve months of use, and gross-cumulative lifetable event and continuation rates over a twelve-month follow-up period.

II. Materials and Methods

Study Products

The TCu 200 is a T-shaped IUD made of polyethylene with barium sulfate added for x-ray detectability. It is wound with copper wire on the stem providing a surface area of 200 mm². The cross arm is 32 mm in width and the vertical arm is 36 mm in length. The proximal end of the IUD stem is provided with two marker threads.

The TCu 380A is also a T-shaped device made of polyethylene with barium sulfate. It has two 33 mm² solid copper sleeves on each transverse arm and 314 mm² of copper wire wound tightly around the vertical stem. This increased copper surface area, the most found on any commercially available copper IUD, is expected to improve the efficacy of the TCu 380A over the standard TCu 200 IUD. The device is also 32 mm wide and 36 mm long but has a plastic ball at the bottom of the vertical stem to guard against

cervical penetration. A polyethylene filament is tied through the ball which provides two marker threads. Studies conducted by the World Health Organization have demonstrated an expanded lifespan of six years for the IUD. At the time of this study however, the US FDA approved lifespan for this device was four years.

Selection Criteria

Women 18 to 40 years old who were healthy, sexually active, seeking intrauterine contraception, \geq 40 days postpartum, and willing to rely solely on the IUD for contraception were admitted into the trial. Other criteria for inclusion were that general and pelvic examinations, including Pap smear, were normal and the women had no active sexually transmitted diseases, undiagnosed vaginal bleeding or allergy to copper. Candidates for this study were excluded if they had a history of ectopic pregnancy, an abnormal pap smear (3 months or less prior to study), and history or evidence of clinically significant gastrointestinal or renal disease.

Two hundred and seventy-nine women were enrolled over a 27-month period beginning in June 1986. Although the recruitment period was extended twice to accommodate slow admissions, the proposed goal of 300 study participants was not met. By random allocation, 139 received the TCu 380A IUD and 140 women received the TCu 200 IUD. Two allocation errors occurred when one woman received the TCu 380A instead of the TCu 200 and another received

the TCU 200 instead of the TCU 380A. These women are grouped in the study according to which IUD they received and are then included in the analysis. All women gave informed consent before admission and agreed to return to the clinic for follow-up visits.

Admission Procedures

According to the protocol, insertions were to be performed no sooner than 40 days after the end of the most recent pregnancy. Women who had their IUD inserted at ≤ 39 days after pregnancy end were considered major protocol violations and although they participated in the study, they are not included in the efficacy analysis. In this study, two women in the TCU 200 group had their IUDs inserted at 37 and 38 days after pregnancy. Also, two women in the TCU 380A group exceeded the age criteria listed in the protocol; one woman was 41 years old and one was 42 years old. These four women were permitted to continue in the study, but the postpartum women are excluded from the efficacy analysis as major protocol violations.

Patients were requested to return for follow-up at 1, 3, 6 and 12 months after insertion of their IUD or at any time complications occurred. Women were terminated from the study if pregnancy occurred, if their IUD was partially or totally expelled or if their IUD was removed for any reason. Study devices that were partially or totally expelled after insertion were not to be reinserted.

Data Analysis

Data were recorded on standard case report forms by clinic staff and sent to FHI for processing and analysis. Differences in categorical data were assessed using the chi-square test of significance and comparisons of means using the t-test. Rates of discontinuation for specific reason were calculated using the lifetable method [1]. Single decrement gross lifetable rates were compared using the log rank statistic which permits the overall comparison of cumulative lifetable event rates [2]. Statistical significance was set at $p < 0.05$. For this study, the power to detect a four percent difference in groups for an event which occurs in five percent of the participants of one group is less than .40 for the number of patients admitted. The power to detect a five percent difference is less for comparisons of more common events and for the group comparisons made on outcome variables measured after attrition.

III. Patient Characteristics

Selected sociodemographic characteristics were similar for both groups (Table I). Mean age was 31.1 years for women in the TCu 380A group and 30.4 years in the TCu 200 group. All women were parous; the median number of live births was 4.8 for the TCu 380A group and 4.5 for the TCu 200 group. Over 59 percent of the women in both groups reported using no contraceptive method during the month prior to admission into the study. When reported however, the most frequently used methods were IUDs and withdrawal/rhythm.

IV. Results

Complications/Complaints

Complications and complaints reported during the study period are summarized in Table II. At admission a total of eleven women were diagnosed with inflammations or infections of either the vagina, cervix or vulva: seven in the TCU 380A group and four in the TCU 200 group. Three cervical lacerations occurred during insertion in the TCU 380A group and one in the TCU 200 group. Mild pelvic pain was reported by seven women in the TCU 380A group and by eight women in the TCU 200 group (data not shown). No statistically significant differences between the two groups were noted for these complications and complaints.

One hundred and eighteen women in the TCU 380A group and 121 in the TCU 200 group returned for at least one follow-up visit. Two women in the TCU 380A group and one woman in the TCU 200 group were hospitalized during the study. One woman in the TCU 380A group was hospitalized for seven days (three months after insertion) because of hemorrhaging due to degeneration of a uterine fibroid; she was discontinued from the study. The other TCU 380A user was hospitalized for three days (six months after insertion) for a non-IUD related condition; she continued in the study. The woman in the TCU 200 group was diagnosed with malaria three months after insertion; she was hospitalized for three days and continued in the study.

Table II also includes data on bleeding/pain complaints at follow-up. These included intermenstrual pelvic pain reported by 46 TCu 380A users and 44 TCu 200 users; intermenstrual spotting, experienced by 16 users in each group; and intermenstrual bleeding reported by 10 TCu 380A users and 13 TCu 200 users. Dysmenorrhea was reported by 43 women in the TCu 380A group and 47 women in the TCu 200 group. No statistically significant differences between the two groups were noted for any of these complaints.

Fifty-two women were diagnosed with other inflammations or infections: 19 cases of vaginitis in the TCu 380A group and 21 in the TCu 200 group, seven cases of cervicitis in the TCu 380A group and three in the TCu 200 group, and two cases of staphylococcus in the TCu 200 group (Table II). A total of fourteen women were diagnosed with a sexually transmitted disease (STD); the most frequent report was for trichomoniasis, diagnosed for three women in the TCu 380A group and seven women in the TCu 200 group. One case of salpingitis was reported among TCu 380A users. No statistically significant differences between the two groups were noted for any of these conditions.

Termination Events

Table III summarizes participant's status at the end of twelve months of use and Table IV presents the gross-cumulative lifetable rates for the termination events. The two postpartum women were excluded from the efficacy analysis and data for 139

TCu 380A users and 138 TCu 200 users were analyzed. IUD comparisons were made on the basis of various termination rates. Pertinent terminations (those which are method-related to efficacy and acceptability of the IUD) include accidental pregnancy, expulsion, removal for bleeding or pain and removals for other medical reasons. Other medical reasons include (but are not limited to) uterine perforation and infection. Non-pertinent termination reasons include planning a pregnancy and removals for other personal reasons (e.g. husband's objections or no longer need for contraception).

One accidental pregnancy was reported in the TCu 200 group yielding a twelve-month gross-cumulative lifetable rate of 1.0 per 100 women. This user became pregnant approximately four months after insertion; the estimated gestational age was 14 weeks when the pregnancy was confirmed. The pregnancy outcome was a live birth.

IUDs were expelled or displaced in seven TCu 380A users and two TCu 200 users. The twelve-month gross-cumulative lifetable rates were 6.8 per 100 women for the TCu 380A group and 1.7 per 100 women for the TCu 200 group. The difference in these rates was not statistically significant.

One woman in the TCu 380A group and three in the TCu 200 group had their IUDs removed because of bleeding and/or pain. These removals yielded gross-cumulative lifetable rates of 1.0 and 2.7

per 100 women, respectively. The difference in rates was not statistically significant.

One TCU 200 user had her IUD removed to plan a pregnancy which resulted in a twelve-month gross-cumulative lifetable rate of 1.3 per 100 women. The differences in both sets of lifetable rates were not statistically significant. A woman in the TCU 380A group had her IUD removed for personal reasons because she was changing her residence and could not continue in the study. The twelve-month gross-cumulative lifetable rate was 1.1 per 100 women.

The rates for total terminations at twelve months were 8.8 per 100 women for the TCU 380A group and 6.6 per 100 women for the TCU 200 group. This difference was not statistically significant.

Lifetable rates for continuation with the IUD and follow-up percentages were calculated for the 277 interval patients (Table V). Continuation rates are defined as 100 minus the total termination rate and indicate the user did not terminate from the trial. Twenty-one women in the TCU 380A group and 19 in the TCU 200 group did not return for follow-up after their admission into the study. At twelve months the continuation rates were 91.2 per 100 women for the TCU 380A group and 93.4 per 100 women for the TCU 200 group. The difference between these rates was not statistically significant. Follow-up status (Table V) is defined

as the percentage of women not previously terminated who returned for a follow-up visit. These percentages were at or above 54% for both groups over the duration of the study.

V. Special Studies

To determine if an IUD is effective, a clinical trials participant needs to be sexually active. At each follow-up visit the frequency of women's intercourse was recorded (Table VI). The frequency of intercourse was similar between the two groups; it increased between the first and second follow-up visits. Perhaps it took some time for the women to feel safe from pregnancy before resuming their normal sex life.

VI. Summary

From June 1986 to September 1988, IUDs were inserted in 279 women participating in a clinical trial at the University of Yaoundé in Yaoundé, Cameroon. By the process of random allocation, 139 women had a TCu 380A IUD inserted and 140 women a TCu 200 IUD. Two of the 140 women in the TCu 200 group were excluded from the efficacy analysis because their IUDs were inserted at ≤ 39 days after pregnancy end. Participants in the two groups were similar with respect to selected sociodemographic characteristics. Insertion-related complaints were few; those reported were mainly for mild pelvic pain and cervical lacerations.

One hundred and eighteen women in the TCU 380A group and 121 in the TCU 200 group returned for at least one follow-up visit . The most frequently reported menstrual complaints in either group were for dysmenorrhea and intermenstrual pelvic pain. Over twenty-one percent of the women in each group were diagnosed with inflammation or infections, six of these women had infections at admission. The difference between each group for inflammations/infections was not significant. The most frequent termination event in each study group was due to expulsion or displacement. Although the follow-up percentages were low, a total of 109 women in the TCU 380A group and 112 women in the TCU 200 group continued use of their IUD after the twelve-month study period had ended.

Although these data cannot be considered definitive, this study does suggest that the TCU 380A is no different in terms of safety and effectiveness, for this population of users, than the TCU 200. A majority of the women in both groups elected to continue using the assigned IUD as their method contraception after the trial was completed. Although no significant differences between the two IUDs were observed in the incidence of terminations or complications, the power to detect a clinically important difference was low in this study. Power was even less for the comparison of follow-up parameters, such as pelvic pain and PID, since the lost to follow-up percentage was high.

Unlike the TCU 200, the TCU 380A does offer the benefit of a longer IUD lifespan. A longer lifespan would allow for fewer requests for removal over time, longer contraceptive protection, and for a longer time span between births. The value of this longer IUD lifespan suggests that the TCU 380A should be considered for use in family planning programs.

References

1. Potter R. Use-effectiveness of intrauterine contraception as a problem in competing risks. In Freeman R, Takeshita J (eds), *Family Planning in Taiwan*. Princeton, New Jersey: Princeton University Press, 1969.
2. Azen S, Roy S, Pike M, Casagrande. Some suggested improvements to the current statistical methods of analyzing contraceptive efficacy. *Journal of Chronic Diseases* 29, 1976.

Table I

**Selected Sociodemographic Characteristics
Comparative Study of the TCU 380A vs. the TCU 200 IUD
Yaoundé, Cameroon**

| Characteristics | TCu 380A (N=139) | | TCu 200 (N=140) | |
|---|---------------------|------|--------------------|------|
| | No. | % | No. | % |
| Age (years) | | | | |
| <20 | 4 | 2.9 | 3 | 2.1 |
| 20-24 | 13 | 9.4 | 16 | 11.4 |
| 25-29 | 42 | 30.2 | 47 | 33.6 |
| 30-34 | 47 | 33.8 | 47 | 33.6 |
| 35+ | 33 | 23.8 | 27 | 19.3 |
| Mean | 31.1 | | 30.4 | |
| Total Number of Live Births | | | | |
| 1 | 9 | 6.5 | 7 | 5.0 |
| 2 | 14 | 10.1 | 15 | 10.7 |
| 3 | 21 | 15.1 | 19 | 13.6 |
| 4 | 16 | 11.5 | 28 | 20.0 |
| 5 | 28 | 20.1 | 32 | 22.9 |
| 6 | 16 | 11.5 | 19 | 13.6 |
| 7 | 20 | 14.4 | 10 | 7.1 |
| 8+ | 15 | 10.8 | 10 | 7.1 |
| Median | 4.8 | | 4.5 | |
| Use of a Contraceptive in the Past Month | | | | |
| None | 82 | 59.0 | 86 | 61.4 |
| IUD | 33 | 23.7 | 26 | 18.6 |
| Withdrawal/Rhythm | 15 | 10.8 | 10 | 7.1 |
| Orals | 6 | 4.3 | 12 | 8.6 |
| Barriers | 2 | 1.4 | 5 | 3.6 |
| Injectables | 1 | 0.7 | 1 | 0.7 |

Table II

Complications/Complaints Reported at Insertion and Follow-up*
Comparative Study of the TCU 380A vs. TCU 200 IUDs
Yaoundé, Cameroon

| Complication/Complaint | TCu 380A No. | TCu 200 No. |
|------------------------------------|-----------------|----------------|
| Total Women at Admission | N=139 | N=140 |
| Cervical Laceration | | |
| No treatment | 2** | 1** |
| Packing | 1*** | 0 |
| Inflammations/Infections | | |
| Cervical Erosion | 3 | 1 |
| Vaginitis | 1 | 1 |
| Candidiasis | 1 | 1 |
| Cervicitis | 1 | 0 |
| Mycosis | 1 | 0 |
| Condyloma | 0 | 1 |
| Total Women Followed-up | N=118 | N=121 |
| Hospitalization | 2 | 1 |
| Menstrual Complaints | | |
| Dysmenorrhea | 43 | 47 |
| Intermenstrual: | | |
| Pelvic Pain | 46 | 44 |
| Spotting | 16 | 16 |
| Bleeding | 10 | 13 |
| Other Inflammation/Infection | | |
| Vaginitis | 19 | 21 |
| Cervicitis | 7 | 3 |
| Staphylococcus | 0 | 2 |
| Sexually Transmitted Disease (STD) | | |
| Trichomonas | 3 | 7 |
| Chlamydia | 0 | 1 |
| Gonorrhoea | 1 | 0 |
| Genital Syphilis | 0 | 1 |
| Condyloma | 0 | 1 |
| Pelvic Inflammatory Disease (PID) | | |
| Salpingitis | 1 | 0 |

* More than one event may be recorded for a woman.

** Mechanism of laceration was a tenaculum.

*** Mechanism of laceration was cervical forceps.

Table III

Participant Status After Twelve Months of Use
Comparative Study of the TCU 380A vs. TCU 200 IUDs
Yaoundé, Cameroon

| Characteristics | TCu 380A (N=139) | | TCu 200 ¹ (N=138) | |
|-----------------------------|---------------------|----------------|---------------------------------|------|
| | No. | % ² | No. | % |
| Continuing | 109 | 78.4 | 112 | 81.2 |
| Accidental Pregnancy | 0 | - | 1 | 0.7 |
| Expulsion | 7 | 5.1 | 2 | 1.4 |
| Removal: | | | | |
| Pain and/or bleeding | 1 | 0.7 | 3 | 2.2 |
| Planned pregnancy | 0 | - | 1 | 0.7 |
| Personal reasons | | | | |
| Changed address | 1 | 0.7 | 0 | - |
| Not Followed-up | 21 | 15.1 | 19 | 13.8 |

¹ Excludes the two TCU 200 postpartum cases.

² The percentages may not total 100 due to rounding.

Table IV
Gross-Cumulative Lifetable Events Per 100 Women
Comparative Study of the TCU 380A vs. TCU 200 IUDs
Yaoundé, Cameroon

| Termination Type and Period | TCu 380A Rate S.E. ² | TCu 200 ¹ Rate S.E. |
|---|---------------------------------------|--------------------------------------|
| Accidental Pregnancy | | |
| 3 months | 0.0 ± 0.0 | 0.0 ± 0.0 |
| 6 months | 0.0 ± 0.0 | 1.0 ± 1.0 |
| 12 months | 0.0 ± 0.0 | 1.0 ± 1.0 |
| Expulsion/Displacement | | |
| 3 months | 4.4 ± 1.9 | 1.7 ± 1.2 |
| 6 months | 5.4 ± 2.2 | 1.7 ± 1.2 |
| 12 months | 6.8 ± 2.5 | 1.7 ± 1.2 |
| Removal for Bleeding/Pain | | |
| 3 months | 1.0 ± 1.0 | 2.7 ± 1.5 |
| 6 months | 1.0 ± 1.0 | 2.7 ± 1.5 |
| 12 months | 1.0 ± 1.0 | 2.7 ± 1.5 |
| Removal for planning pregnancy | | |
| 3 months | 0.0 ± 0.0 | 0.0 ± 0.0 |
| 6 months | 0.0 ± 0.0 | 0.0 ± 0.0 |
| 12 months | 0.0 ± 0.0 | 1.3 ± 1.2 |
| Removal for other personal reasons | | |
| 3 months | 0.0 ± 0.0 | 0.0 ± 0.0 |
| 6 months | 0.0 ± 0.0 | 0.0 ± 0.0 |
| 12 months | 1.1 ± 1.1 | 0.0 ± 0.0 |
| Total terminations | | |
| 3 months | 5.4 ± 2.1 | 4.4 ± 1.9 |
| 6 months | 6.3 ± 2.3 | 5.4 ± 2.1 |
| 12 months | 8.8 ± 2.8 | 6.6 ± 2.4 |

¹ Excludes the two TCU 200 postpartum cases.

² Standard Error; no statistically significant differences were detected. Lost to follow-up cases are censored by the lifetable procedure.

Table V

**Rate of Continuation and Follow-up Percentage
Comparative Study of the TCu 380A vs. TCu 200 IUDs
Yaoundé, Cameroon**

| Termination Type and Period | TCu 380A | TCu 200 ¹ |
|--|----------|----------------------|
| Continuation Lifetable Rate² | | |
| 3 months | 94.6 | 95.6 |
| 6 months | 93.7 | 94.6 |
| 12 months | 91.2 | 93.4 |
| Follow-up Percentage³ | | |
| 3 months | 77.8 | 78.5 |
| 6 months | 71.2 | 67.4 |
| 12 months | 57.3 | 55.0 |

¹ Excludes the two TCu 200 postpartum cases.

² The continuation rate is defined as 100 minus the total termination rate (refer to Table IV). No statistically significant differences were detected. Lost to follow-up cases are censored by the lifetable procedure.

³ The percentage of women returning for follow-up who have not been previously terminated.

Table VI
Special Studies
Comparative Study of the TCU 380A vs. TCU 200 IUDs
Yaoundé, Cameroon

| Frequency of Intercourse in Last Four Weeks | Percent ¹ of Women by Group ² | | | | | | | |
|--|---|--------------|-------------|-------------|-------------|-------------|--------------|--------------|
| | FU 1 | | FU 2 | | FU 3 | | FU 4 | |
| | <u>A</u> | <u>B</u> | <u>A</u> | <u>B</u> | <u>A</u> | <u>B</u> | <u>A</u> | <u>B</u> |
| | N=102 | N=103 | N=86 | N=84 | N=78 | N=73 | N=139 | N=138 |
| 0 | 7.8 | 20.4 | 5.8 | 6.0 | 5.1 | 2.7 | 4.3 | 2.2 |
| 1-5 | 35.3 | 24.3 | 26.7 | 20.2 | 24.3 | 20.5 | 25.2 | 29.0 |
| 6-10 | 29.4 | 25.2 | 36.0 | 40.5 | 28.2 | 39.7 | 70.5 | 68.8 |
| 11-15 | 18.6 | 22.3 | 23.2 | 22.6 | 25.6 | 28.8 | 0.0 | 0.0 |
| 16-20 | 8.8 | 6.8 | 8.1 | 8.3 | 16.7 | 8.2 | 0.0 | 0.0 |
| 21+ | 0.0 | 1.0 | 0.0 | 2.4 | 0.0 | 0.0 | 0.0 | 0.0 |

¹ The percentages may not total 100 due to rounding.

² Group A consists of TCU 380A users and Group B consists of TCU 200 users.

Data Quality Statement

The progress of this study was slow as it had to overcome several hurdles in the beginning. The admissions took 27 months to complete and the actual recruitment period of twelve months was extended twice to accommodate the slow process. There was a temporary shortage of IUDs because study IUDs were also being used for other patients. Informed consent procedures were followed and there were two random allocation errors.

Four protocol violations occurred during the admission process: two women in the TCU 380A group exceeded the age criteria, one woman was 41 years old and one was 42 years old; two women in the TCU 200 did not meet the interval status criteria, their IUDs were inserted at 37 and 38 days after pregnancy. Pap smear results from admission were available for each woman, but these results were coded onto subsequent follow-up forms resulting in coding errors. The investigator was subsequently told that Pap smear results should be coded only when results were received. The investigator was also advised to periodically check the follow-up log book against the forms to verify that all women returned for their scheduled follow-up visit.

Pursuant to the protocol, this consultant report only analyzed events occurring within the twelve month study period. Terminations that occurred after twelve months were not analyzed and the women were considered as continuing with the IUD. Nine terminations in the TCU 380A group and twelve in the TCU 200 group were reported during the 13-24 month interval. These terminations included: one expulsion or displacements in the TCU 200 group, three for bleeding and/or pain in the TCU 380A group and one in the TCU 200 group, one for other medical reasons in the TCU 380A and two in the TCU 200 group, and five for planning a pregnancy in the TCU 380A group and eight in the TCU 200 group.

Note: This statement is provided to the investigator to help him set the study's results in the proper context. The quality of the data collected may affect the validity of the stated results.