

# Effectiveness, Safety, and Acceptability of a Copper Intrauterine Device (CU Safe 300) in Type I Diabetic Women

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**OBJECTIVE**— To evaluate the long-term effectiveness and safety of a copper intrauterine device fulfilling modern standards in type I diabetic women compared with nondiabetic women.

**RESEARCH DESIGN AND METHODS**— Type I diabetic women ( $n = 59$ , age  $27 \pm 5$  yr, duration of diabetes  $12 \pm 8$  yr,  $HbA_{1c}$   $7.0 \pm 1.2\%$ , 78% nulliparous women) were prospectively evaluated at 3, 6, 12, 24, and 36 mo by a gynecological exam and a standardized questionnaire after insertion of the intrauterine device (CU Safe 300, 300 mm<sup>2</sup> of copper). A group of nondiabetic women ( $n = 1150$ ) of comparable age and parity evaluated according to the same study protocol served as a control group.

**RESULTS**— In the diabetic women (1754 cumulative months of use), events leading to termination of the intrauterine device during the 1st yr (691 women-mo) were one accidental pregnancy, one expulsion, one removal for pain, two removals for bleeding, and one removal for planned pregnancy. Events during the 2nd (593 women-mo) and 3rd yr (470 women-mo) were zero and one accidental pregnancy, one and two removals for bleeding, one and one removal for pain, one and one removal for other medical reasons, and two and two removals for planned pregnancy, respectively. No case of pelvic inflammatory disease was diagnosed in the diabetic group, and one case was diagnosed in the nondiabetic group (28,369 mo of cumulative use). Events leading to termination of the intrauterine device per women observed per year and continuation with the intrauterine device after each year of use were comparable in the diabetic and nondiabetic groups for the 1st, 2nd, and 3rd yr.

**CONCLUSIONS**— These results, although preliminary because <100 diabetic women were studied, indicate that the intrauterine device CU Safe 300 is as effective, safe, and well-tolerated in diabetic as in nondiabetic women. Specific objections to the use of intrauterine devices in type I diabetic women do not seem to be justified for modern, copper-medicated models.

For many diabetic women, the choices for reversible contraception are limited. Hormonal contraception with estrogen-progestogen preparations might increase the risk for vascular complications especially in the presence of microangiopathies (1,2). The low-dose progestogen pill, although recommended by many diabetologists, is frequently not well-tolerated because it is associated with a high rate of menstrual irregularities (1,2). Vaginal barrier methods and natural methods might be unacceptable because of their high failure rate, because the avoidance of an unplanned pregnancy is even more important for women with diabetes than for women without diabetes (2). Intrauterine contraception could represent an acceptable method of contraception for diabetic women when the improved models of copper-medicated IUDs are used, because in nondiabetic and in diabetic women, such devices have already been proven to be safer and more effective than older models (3–6). However, largely based on studies using nonmedicated IUDs and older models of medicated IUDs (7), concern exists about the safety and efficacy of IUDs in women in general and in diabetic women in particular (1,8,9). Widespread belief exists that diabetic women are more prone to pelvic infections associated with IUD use than nondiabetic women (8). So far, no studies have evaluated the safety and efficacy of IUDs in diabetic women beyond 1 yr of use (1,9–12).

To evaluate whether specific objections to IUD use in diabetic women are warranted for modern, copper-bearing models, we have prospectively studied the safety, efficacy, and acceptability of a newly developed copper IUD in type I diabetic women compared with a group of nondiabetic women.

## RESEARCH DESIGN AND METHODS

From January 1986 to January 1991, all type I diabetic women who attended the

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IUD, intrauterine device; PID, pelvic inflammatory disease; type I diabetes, insulin-dependent diabetes mellitus; HPLC, high-performance liquid chromatography; CI, confidence interval.



Table 1—Clinical characteristics of diabetic and nondiabetic women

	Diabetic women	Nondiabetic women
Age (yr)	27 ± 5	28 ± 5
Duration of diabetes (yr)	12 ± 8	
Nullipara (%)	78	74
Age-group (yr)		
15–19	5 (8)	37 (3)
20–24	18 (31)	274 (24)
25–29	19 (32)	337 (29)
30–34	11 (19)	245 (21)
35 plus	6 (10)	257 (22)
Total	59	1150

Data are means ± SD or n (%).

practice of two gynecologists (K-H.K. and P.A. Meier-Oehlke) for consideration of intrauterine contraception were asked to participate in the study after they had been informed about potential risks in detail (2). Women with contraindications such as uterine abnormalities, evidence of PID, anemia, or with a history of ectopic pregnancy and PID were excluded ( $n = 2$ ). IUD performance in terms of accidental pregnancy, expulsion, and removal for medical and personal reasons was ascertained at follow-up visits, scheduled at 3, 6, 12, 24, and 36 mo after insertion. Thereafter, the observation period of the study was terminated, the IUD removed and replaced if indicated. Initial and follow-up evaluations consisted of a gynecological examination, including ultrasound imaging of the IUD in utero and a standardized questionnaire about the reproductive, contraceptive, menstrual, and medical history. The study was conducted according to the Declaration of Helsinki.

The 59 type 1 diabetic women participated in the study after signing an informed consent form. Before entering the study the following methods of contraception were used by the women: oral hormonal contraception (44%), IUDs (37%), vaginal barrier methods (14%), and no contraception (5%). The participants (97% of whom indicated one steady sexual partner) had been referred to the gynecological study center by our

diabetes center ( $n = 34$ ) or by other diabetologists and internists in and around Düsseldorf. In 47 (80%) of diabetic women, glycemic control during the study period could be assessed based on at least two values of  $HbA_{1c}$  during the study. These patients had an  $HbA_{1c}$  of  $7.0 \pm 1.2\%$  (HPLC, Biorad, Richmond, CA) (nondiabetic range 4.2–5.5%). Of 45 women in whom the status of diabetic microangiopathic complications could be assessed, 15 (33%) had clinically apparent microangiopathies: background retinopathy ( $n = 9$ ), laser-treated proliferative retinopathy ( $n = 6$ ), incipient nephropathy ( $n = 3$ ), and overt nephropathy ( $n = 3$ ). In 8 patients, the last follow-up examination was performed by their local gynecologist and reported to us in detail. These results were included in the study.

A control group of nondiabetic women ( $n = 1150$ ) was prospectively followed by the same gynecologists according to the same study protocol. The 1-yr results for the nondiabetic women have been published previously (14). The clinical characteristics of diabetic and nondiabetic women are shown in Table 1. The nondiabetic group was comparable with the diabetic group in terms of age, parity, and methods of contraception used before entering the study.

The IUD used in this study (CU Safe 300, Prosan International B.V., The Netherlands) has been developed based on uterine cavity measurements in 714

women of fertile age. Special properties of the IUD are as follows: copper wire surface  $300 \text{ mm}^2$ , fundus-seeking mechanism, dimensional compatibility to uterine cavity, no anchoring protrusions, monofilament integrated in the shaft without a knot, low plastic surface area, and thin inserter tube (radius  $3 \text{ mm}^2$ ) without a plunger (13).

Controlled women-months of use and events leading to termination of the IUD were defined and evaluated according to the modified criteria for intrauterine contraception by Tietze and Lewitt (14) using life table analysis (Lifetest, SAS, Cary, NC) in the diabetic group. Results are given as single events and as rates (events/100 women-yr). In the diabetic women, rates were calculated by extrapolating the events in the respective year of observation to 100 women-yr. Events per women observed in each year in the diabetic and nondiabetic groups were compared with the use of the  $\chi^2$  or Fisher's exact test.

## RESULTS

Table 2 shows the number of events and rates for the 1st, 2nd, and 3rd yr after insertion of the IUD in the groups of diabetic and nondiabetic women.

### Accidental pregnancies and expulsions

Two diabetic women (24 and 21 yr of age) conceived with the IUD in situ, one at 12 and one at 32 mo after insertion of the IUD. Both pregnancies were diagnosed within 9 wk of conception. In the nondiabetic women, 21 pregnancies were recorded with the IUD located either intrauterine or partly intracervically as confirmed by ultrasound. None of the pregnancies was ectopic. Accidental pregnancies per women observed per year were comparable between diabetic and nondiabetic women for the 1st, 2nd, and 3rd yr. One partial expulsion (visibility of the IUD shaft at the external os) occurred in one diabetic woman at 5 mo after insertion, and none in the additional observation period.



Table 2—Events leading to termination of the IUD

	Diabetic women (n = 59)			Nondiabetic women (n = 1043)		
	1st yr	2nd yr	3rd yr	1st yr	2nd yr	3rd yr
n	59	52	47	1043	876	687
Follow-up						
Accidental pregnancy	1 (1.7)	0	1 (2.6)	5 (0.5)	10 (1.3)	6 (1.0)
Expulsion	1 (1.7)	0	0	5 (0.5)	0	1 (0.2)
Medical removals						
Bleeding	2 (3.5)	1 (2.0)	2 (5.1)	37 (3.8)	20 (2.5)	13 (2.2)
Pain	1 (1.7)	1 (2.0)	1 (2.6)	13 (1.3)	4 (0.5)	5 (0.8)
Infection	0	0	0	0	1 (0.1)	0
Other medical	0	1 (2.0)	1 (2.6)	8 (0.8)	5 (0.6)	3 (0.5)
Nonmedical removals						
Planning of pregnancy	1 (1.7)	2 (4.0)	2 (5.1)	28 (2.9)	47 (5.9)	46 (7.8)
Controlled months of use	691	593	470	11,684	9596	7089
Cumulated continuation rate (%)†	91 (CI 84–98)	81 (CI 71–91)	68 (CI 55–80)	91 (CI 89–93)	81 (CI 79–84)	71 (CI 68–74)
Lost to follow-up (%)	0			9		

(Rates) = events during the year of follow-up ÷ cumulative months of use × 1200 mo (events/100 women-yr). Events per women observed per year were not significantly different between diabetic and nondiabetic women for the 1st, 2nd, and 3rd yr, respectively.

†Determined by life table analysis.

#### Medical removals and continuation rates

In the diabetic women, the removals per women followed per year for increased menstrual and additional uterine bleeding and pain, respectively, were equally low compared with the nondiabetic women. One woman with diabetic nephropathy had the IUD removed for an ovariectomy and hysterectomy to remove a benign ovarian tumor. As judged by history, clinical examination, and laboratory tests, no cases of PID were diagnosed in the diabetic group, and one case was diagnosed in the nondiabetic group. In one diabetic woman, the IUD was removed in an outside hospital because of pain suggestive of PID. However, normal laboratory exams and normal findings on laparoscopy did not subsequently confirm the diagnosis of PID. The percentage of women continuing on IUD after the 1st, 2nd, and 3rd yr was similarly high in the diabetic and nondiabetic groups.

#### CONCLUSIONS

In this study, the long-term use of a newly developed copper-bearing IUD in

59 type I diabetic women showed similarly favorable results compared with a large group of nondiabetic women of comparable age and parity. In both groups, most of the women were nulliparous and in an age-group with high fertility. Our study confirms the results of the only other study with modern copper IUDs in diabetic women (12). In that study by Skouby et al. (12), 103 diabetic women using predominantly the T CU 200 IUD were followed for 1 yr; the Pearl index was 1.0, which is comparable with the extrapolated index of 1.7 in our study and well within the range of Pearl indexes of 0.6–2.0 reported for other state-of-the-art copper IUDs in nondiabetic women (3).

In our study, <100 women were included so that classic rates (events/100 women-yr, i.e., Pearl index) could only be extrapolated, and CIs for rates as determined by life table analysis were wide. Nevertheless, we suggest that, despite the small number of participants, our results give valid new information about the long-term use of copper-medicated IUDs in diabetic women, because the cumulative time of use of 1754 mo was

longer than that evaluated in any of the four previous studies on IUD use in diabetic women (9–12).

Four of five studies (including our study) and broad clinical experience reported by centers in France (2) and Denmark (4) did not find differences in the performance of IUDs in diabetic and nondiabetic women. However, on the basis of the available data, small differences cannot be excluded with certainty because of insufficient statistical power.

Skouby et al. (12) did not find differences in corrosion patterns examining Nova Ts and Multiload IUDs removed from diabetic and nondiabetic women after 1 yr of use. However, with prolonged use the time-dependent corrosion of an IUD (leading to decreased spermicidal efficacy mediated by the copper-releasing capacity of an IUD) conceivably might be influenced by the level of glycemic control. In our study, most patients, including the two patients who became pregnant, were in good to moderate glycemic control. Data on glycemic control in the other studies are not given or are inconclusive (9–12). Obviously, based on these data, the issue



whether the level of glycemic control has any influence on the efficacy of IUDs in diabetic women cannot be resolved.

The attitudes put forth by opinion leaders toward intrauterine contraception and the frequency of IUD use in diabetic women vary widely between countries, in parallel to attitudes about intrauterine conception in nondiabetic women (1,2,4). In our study, the majority of women were nulliparous, a group of women in whom IUDs are rarely used, largely because nulliparous women showed a higher rate of PID in older studies using nonmedicated IUDs (7). However, studies that investigated IUDs with high copper-releasing capacity in populations not exposed to an increased risk for sexually transmitted diseases have, if at all, found only a slightly increased risk for PID and an excellent outcome for subsequent fertility, even in women in whom the IUD had been removed because of complications (3,5,15). Moreover, none of the studies examining intrauterine contraception in diabetic women compared with nondiabetic women showed an excess incidence of PID in diabetic women (9-12). In fact, in our study, no case of PID was diagnosed, and in the study of Skouby et al. (12), one single case of PID as judged by clinical methods was diagnosed.

The favorable results as to the safety of modern copper IUDs should make their use less restrictive also in nulliparous diabetic women who do not have other contraindications. For women with diabetic microangiopathies, this might be the only acceptable method of contraception (2,4). Although not observed in our study, the risks of IUDs (ectopic pregnancy and PID), which might remain to a minor degree even with modern IUDs, should be presented in great detail, especially to the nulliparous woman, when giving contraceptive advice (2).

In our study, the continuation rate among diabetic and nondiabetic women was high, and the removals for

bleeding and pain tended to be lower than in most studies in nondiabetic women with other modern IUDs (3). However, note that, in this study, 33% of the women had used an IUD previously and that diabetic women who are advised against the use of combined hormonal contraception might more readily accept unpleasant side effects.

In summary, under the conditions of this study, the CU Safe 300 IUD is as effective, safe, and well-tolerated in diabetic as in nondiabetic women. Specific objections as to the efficacy and safety of IUDs in diabetic women compared with nondiabetic women do not seem to be justified for modern, copper-medicated IUDs.

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