COMPARATIVE MULTICENTRE TRIAL OF THREE IUDS INSERTED IMMEDIATELY FOLLOWING DELIVERY OF THE PLACENTA

World Health Organization
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ABSTRACT

A multinational comparative trial of three IUDs (Copper 7, Lippes loop size D and the Postpartum T) randomly inserted immediately following delivery of the placenta was conducted in six centres. A total of 841 women entered the study. As the predetermined termination indices for expulsions were exceeded at six months the trial was prematurely closed. An excess of expulsions during the first 48 hours following insertion was observed for the Lippes loop compared to the other devices. At six months the expulsion rate for the Lippes loop was significantly higher than that for the Copper 7. In addition, the discontinuation rate for the Lippes loop at 12 months was significantly higher than that for the Copper 7. There were no significant differences in either the expulsion rates or the discontinuation rate at six or twelve months between the postpartum T and the other devices. At 12 months the pregnancy rates with all three devices was high; there were no ectopic pregnancies. Considerable between-centre differences were observed, particularly for expulsion rates. Possible reasons for this are discussed and future research lines are suggested.

INTRODUCTION

Insertion of an intrauterine device immediately following delivery of the placenta has many potential advantages for family planning programmes. This is particularly true for those areas where contact with potential family planning acceptors is infrequent and where supervised puerperal care is of short duration. Motivation for the use of fertility regulating methods is usually high at the end of a pregnancy and insertion of an IUD provides immediate fertility regulation without interfering with lactation, as may occur with hormonal methods. In addition, the fact that an IUD is already present confers protection against pregnancy for those who are reducing their breast-feeding and whose time of return to fertility is uncertain. However, balanced against these programmatic advantages, the disadvantages of post-placental IUD insertion might include a high expulsion rate, an unacceptable incidence of pelvic inflammatory disease or a higher than usual uterine perforation and translocation rate.

There have been few reported studies of immediate post-placental insertion of an IUD. Burnhill and Birnberg (1) reported on 134 post-placental insertions of the Birnberg Bow. There were 5 expulsions, either partial or complete, no uterine perforations and one case of endometritis during the study period. Following a favourable report by Rashbaum and Wallach (2) of post-placental insertion of the LEM device, Apelo *et al.* (3) reported on 1359 post-placental insertions of the same device. There was a high (20.6%) expulsion rate at one year; most expulsions occurring during the early months of use. The removal rate for pain and bleeding was low (2.0%) but the pregnancy rate was high (5.0%). Despite these disadvantages, the continuation rate at one year was 70.1%, which compares well with continuation rates for interval insertion of, for example, the copper T-200 and T-300 (4).

Newton *et al.* (5) carried out 274 post-placental insertions of the LEM, Cu-7, and Progestasert using a specially-designed 25-cm inserter. There were no uterine perforations and the expulsion rate was about 7.0% at six weeks. Recently, Laufe *et al.* (6) have reported on post-placental insertion of the Lippes Loop modified by having three short lengths of chromic catgut attached to the superior cross-arm of the device. The life-table expulsion rate at six months was 5.3/100 women.

The present study was initiated by the Task Force on Intrauterine Devices for Fertility Regulation of the WHO Special Programme of Research, Development and Research Training in Human Reproduction. The object of the study was to compare the use-effectiveness of three IUDs, the post-partum copper T, Lippes Loop D and Copper 7, inserted immediately after delivery of the placenta.

MATERIALS AND METHODS

Healthy informed pregnant volunteers aged between 16 and 40 years who were scheduled for a vaginal delivery were recruited prior to delivery in six centres. All subjects consented to enter the study having been informed of the advantages and possible side effects of intrauterine device use, alternative methods and their freedom to withdraw from the study at any time. A total of 841 subjects were recruited. Patients with a recent history of pelvic inflammatory disease or venereal disease treated during the current pregnancy, congenital abnormalities of the uterus or vagina, known or suspected genital tract malignancy, uterine fibroids, or evidence of infection during labour were excluded from the study. All subjects were willing to rely solely on the IUD for fertility regulation and all were exposed to the risk of pregnancy.

Three IUDs were studied, the Copper 7 (Gravigard), the Lippes Loop size D and the Post-partum T (Population Council). The latter is a T-shaped device with two 2-cm long additional arms extending upwards and outwards from the lower end of the vertical limb. The vertical limb is wound with copper wire giving a copper area of 200 mm^2. The devices were randomly allocated within each centre.

Insertion of the IUD took place immediately following expulsion of the placenta. The management of the third stage of labour was according to the usual practice in the centre. In the majority of centres the conventional IUD inserter was used for fundal placement throughout the study. In London a modified inserter 25-cm in length was used (5). In Salvador digital manipulation of the device to the fundus uteri was used for two-thirds of the subjects. In Santiago digital placement was used in five cases. However, in this latter centre, the patients were examined immediately after insertion to determine placement and, if the device was palpable, it was removed and immediately reinserted.

Follow-up of subjects was at 6 weeks post-partum and then at 3, 6, 12 and 24 months. The data were collected on standardized duplicate record forms and one copy was sent to Geneva for centralized data processing. The analysis used the Chiang (7) procedure for the estimation of cumulative net (non-competing risk) life table discontinuation rates and standard errors. Tests of the statistical significance of differences between the cumulative life table rates were based on a Chi-square analysis on one degree of freedom (8). The protocol required that subjects who discontinued during the first 48 hours should be treated as a separate sub-group and not included in the subsequent life table analysis.

Prior to the start of the study, it had been decided that the trial would be discontinued if the lower 95% confidence limit of the pregnancy rate exceeded 3 per hundred woman years, the expulsion rate was greater than 20%, the removal rate greater than 20%, or the perforation rate more than 2%.

RESULTS

Table I shows the number of insertions and the mean age and parity of the three study samples. There were no significant differences between treatment groups with respect to age or parity.

TABLE I: CHARACTERISTICS OF THE STUDY POPULATION

Subject	Post-partum T	Lippes Loop	Copper 7
Number of insertions	287	272	282
Mean age ± SD	24.96 ±5.1	24.5 ±4.8	24.8 ±4.9
Mean parity ± SD	2.3 ±2.76	1.97 ±2.39	2.09 ±2.42
Percent loss to follow-up	17.8%	16.2%	16.0%

A number of women experienced an expulsion within 48 hours of initial insertion. This occurred in 10 (3.5%) cases with the Post-partum T, 22 (8%) with the Lippes Loop and 5 (1.8%) among the Copper 7 subjects. The excess of early expulsions with the Lippes Loop over the Post-partum T and Copper 7 combined was highly significant using the Chi-square test recommended by Azen et al. (9) ($X^2 = 12.5$ with 1 d.f. $P < 0.01$). In accordance with the protocol, these women were withdrawn from the study and were not included in the subsequent life table analysis.

Table II shows the life table event rates and the number of women-months of experience with the three devices over the first year of study. The most important feature is the excessively high expulsion rates which occurred with all three devices within the first six months of use. These expulsion rates exceeded the predetermined criteria that had been set for the termination of the study and, as a result, the trial was prematurely stopped. The expulsion rates with the Copper 7 were significantly lower than with the Lippes Loop devices at 6 and 12 months post-insertion. There were no significant differences between the expulsion rates for the Post-partum T and either the Copper 7 or Lippes Loop. An analysis of expulsion rates by age and parity revealed no consistent trends.

The pregnancy rates were also high with all three devices, but no ectopic pregnancies were observed.

TABLE II: LIFE TABLE DISCONTINUATION RATES AT 6 AND 12 MONTHS AFTER INSERTION

Reasons for discontinuation	Cumulative net life table discontinuation rates per 100 women ± standard errors at 6 and 12 months					
	Post-partum T		Lippes Loop		Copper 7	
	6 months	12 months	6 months	12 months	6 months	12 months
Partial or complete expulsion	39.4 ± 3.2	41.3 ± 3.3	41.3 ± 3.3	44.1 ± 3.4	31.1 ± 2.9	34.8 ± 3.1
Pregnancy	1.6 ± 1.1	5.6 ± 2.3	7.3 ± 2.5	12.1 ± 3.3	1.3 ± 0.9	7.2 ± 2.3
Removal for bleeding and/or pain	3.5 ± 1.6	8.7 ± 2.7	3.5 ± 1.6	4.6 ± 1.9	1.8 ± 1.1	5.2 ± 1.9
Other medical removals	4.0 ± 1.6	5.0 ± 1.9	6.7 ± 2.2	9.0 ± 2.7	0.9 ± 0.6	1.8 ± 1.1
Removals for personal reasons	1.2 ± 0.9	2.4 ± 1.5	1.9 ± 1.4	8.3 ± 3.1	1.9 ± 0.9	6.7 ± 2.1
Total discontinuation rate	45.4 ± 3.3	53.1 ± 3.4	51.9 ± 3.4	60.9 ± 3.4	35.4 ± 3.0	47.7 ± 3.3
Number of woman-months	935	1,497	780	1,196	1,050	1,745

There were no significant differences in the removal rates for bleeding and pain. However, the one year removal rates for "other medical reasons" were significantly lower with the Copper 7 than with Lippes Loop ($X^2 = 6.1$, $p < 0.025$), and this was largely due to an excess of translocations, defined as embedding of the device or altered orientation of the device within the uterine cavity and diagnosed at the time of removal or by radiography. After one year, the translocation rates per 100 women were 2.0 ± 1.2 for the Post-partum T, 2.8 ± 1.7 for the Lippes and 0.9 ± 0.9 for the Copper 7. In Santiago removal of IUDs was found to be difficult in many patients due to embedding of devices in the uterine wall. Problems were also encountered due to fracturing of the Post-partum T at the point where the copper wire was threaded through the stem of the device.

The total discontinuation rates at twelve months were high, and this was particularly the case with the Lippes Loop. There is a statistically significant difference in the total discontinuation rates of the Lippes Loop compared to the Copper 7, ($X^2 = 7.8$, $p < 0.01$), but there were no significant differences between the Post-partum T and the other two devices in this respect.

In a multi-centred trial of this nature it is to be expected that there will be some variation in the results from different clinics. Table III summarizes the main findings from the six centres. The number of subjects recruited into the trial varied, and the results of the pooled data are dominated by three centres; Salvador, Santiago and Szeged which contributed 71% of subjects. Since the high level of expulsions was the main reason for terminating the study and since expulsions were the most frequent event observed, the inter-centre comparisons focused upon this cause of discontinuation. As shown in Table III, there are considerable differences in the expulsion rates between centres, but one centre, Santiago, had particularly low expulsion rates with all three devices compared to the other five centres. Another South American centre, Salvador, also had relatively low expulsion rates with the Copper devices. In order to evaluate this apparent difference between the two Latin American centres and the other European centres, the background characteristics of the subjects, mode of IUD insertion and procedures used for the management of the third stage of labour were examined in detail. These data are summarized in Table III.

TABLE III: INTER-CENTRE VARIATION IN THE NUMBER OF INSERTIONS, EXPULSIONS RATES, AGE AND PARITY OF SUBJECTS, INSERTION PROCEDURES AND USE OF ECBOLICS

Centre	Total number of subjects (all devices)	Cumulative net explusion rates per 100 women ± standard error after 12 months			Mean age ± SD	Mean Parity ± SD	Main insertion procedure	Type of ecbolic used and timing of administration
		Post-partum T	Lippes Loop	Copper 7				
Berlin (West)	88	40.2 ± 9.1	56.4 ±10.7	37.0 ±10.7	27.5 ± 4.2	0.9 ± 0.9	Normal inserter	Ergometrine given post-placentally
Brussels	121	83.6 ± 9.3	77.0 ± 9.5	55.8 ± 8.9	23.8 ± 4.3	2.3 ± 1.2	Normal inserter	Oxytocin after crowning or post-placentally
London	34	39.1 ± 15.7	70.9 ± 19.3	65.0 ± 17.7	24.9 ± 5.5	1.6 ± 1.4	Long post-partum inserter	Oxytocin plus ergometrine with anterior shoulder
Salvador	200	33.3 ± 6.8	49.8 ± 7.9	29.1 ± 6.0	24.9 ± 5.4	2.9 ± 3.4	$^1/_3$ normal inserter, $^2/_3$ digital placement	Ergometrine given post-placentally
Santiago	200	17.7 ± 4.9	10.2 ± 4.0	9.6 ± 4.1	23.7 ± 4.9	1.3 ± 1.3	Normal inserter, 5 cases of digital placement. Immediate reinsertion if placement unsatisfactory	Oxytocin given post-placentally
Szeged	198	58.2 ± 6.6	53.3 ± 6.7	42.0 ± 6.2	25.1 ± 4.8	0.9 ± 0.9	Normal inserter	Oxytocin or ergometrine given post-delivery or post-placentally

DISCUSSION

The expulsion and pregnancy rates encountered in this study were unacceptably high and as a result the trial was prematurely terminated. However, there was substantial inter-centre variation and one centre, Santiago, had low expulsion rates with all three devices.

The lower expulsion rates recorded in Santiago and to a lesser extent in Salvador, cannot be explained on the basis of consistent differences in the age or parity of the study populations. For instance, women in Santiago were of comparable age to women in Brussels and, although the women in Salvador had a higher average parity than the other centres, the subjects in Santiago were of lower parity than the women in Brussels or London (Table III). Furthermore, a separate analysis of expulsion rates by age and parity showed that variations in these demographic characteristics could not account for the magnitude of the inter-centre differences. Most centres (including Santiago) used a normal IUD inserter for the majority of cases. In London, however, a long post-partum inserter was used. Only in Salvador were the majority of insertions performed by digital placement. The ecbolics used varied from centre to centre and it is noteworthy that in the two Latin American centres, ecbolics were usually given post-placentally. Although this procedure was not the universal practice elsewhere, it was used in Berlin (West), Brussels and Szeged for some cases. It is possible that the procedure adopted in Santiago to ensure fundal placement (manual examination and re-insertion where necessary) accounted for the lower expulsion rate in this centre. There were no other major or consistent differences between centres which might account for the variability in the expulsion rates.

Despite some reports of acceptable expulsion rates with post-placental IUD insertion (1, 2, 5, 6), the present study shows that immediate post-placental insertion of the Post-partum Copper T, the Lippes Loop D, and the Copper 7 results in unacceptably high pregnancy and expulsion rates. Further research is needed to assess whether improved insertion procedures or new devices can be developed so as to overcome these problems. In addition, consideration must be given to the management of the third stage of labour with particular regard to the type of ecbolic used and timing of administration.

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