Clinical performance of the Nova-T®380 IUD in routine use by the UK Family Planning and Reproductive Health Research Network*: 12-month report

Michael Cox, FRCOG, MFFP, *Consultant Obstetrician and Gynaecologist*, **Sarah Blacksell**, BA, *Research Fellow Institute of Population Studies, School of Postgraduate Medicine and Health Sciences. University of Exeter, Exeter, UK.*

Correspondence: Michael Cox, Institute of Population Studies, School of Postgraduate Medicine and Health Sciences. University of Exeter, Hoopern House, 101 Pensylvania Road, Exeter EX4 6TD. Tel: 01392 257936; Fax: 01392 490870

(Accepted April 16th, 2000)

Summary

Doctors working in general practice and at family planning clinics throughout the UK who collaborate in the UK Family Planning and Reproductive Health Research Network were responsible for the fitting of 572 Nova-T®380 intra-uterine contraceptive devices (IUDs). The Nova-T® (and formerly the identical Novagard®) IUDs have copper with a surface area of 200 mm². The device used in this study, the Nova-T®380, has copper with a surface area of 380 mm². The purpose of the study was to evaluate the pregnancy and complication rates of this new device, with its increased area of copper, in comparison with other published results, in the clinical setting of British general practice and family planning clinics.

The 12-month cumulative life-table event rates were: pregnancy 0.8, expulsion 5.6, removal for bleeding or bleeding and pain 11.0. The continuation rate was 73.4. The pregnancy rate at 12 months showed good contraceptive performance. The increased surface area of copper was not associated with a reduced pregnancy rate, but as this was not a direct comparative study with the Nova-T®, the influence of the increased area of copper must remain somewhat uncertain. This study found the discontinuation rate for bleeding problems and pain with bleeding to be higher than in other published studies. Other event rates were consistent with other published studies.

***Principal investigators:** V Annandale (Norwich) A Barnett (Exeter), P Barnes (Richmond, London), J Bateman (Portsmouth), J Bland (Nuneaton), D Booker (Newport), R Bradbury (Barnsley), S Brown (Birmingham), G Cardy (Bristol), S Carr (Glasgow), H Cooling (Bristol), M Cox (Nuneaton), J Dewsbury (Birmingham), J Elstub (Richmond, London), S Green (Cumbria), B Hanson (Wiltshire), T Lavery (Wiltshire), A Main (Richmond, London), H Massil (London, CHSL), C Nash (Norwich), R Owen (Taunton), S Randall (Portsmouth), S Richardson (W Yorkshire), S Rowlands (Biggleswade), J Rumsey (Birmingham), J Tattersall (Cumbria), A Taylor (Sheffield), A Thomas (Newport), C Tupper (Cumbria), A Turner (Wiltshire), C Watson (London, CHSL), EM Watt (Bristol).

Key words

intra-uterine contraception, 12-month findings, Nova-T® 380 intra-uterine contraceptive device

Introduction

The copper bearing intra-uterine contraceptive device represents a reliable reversible long-term birth control

Key message points

- At 12 months of use, the Nova-T® 380 has been shown to have a very low pregnancy rate.
- There was a higher than expected removal rate for pain/bleeding.
- Other complications were similar to other published studies.

method. Its performance has been well documented with regard to contraceptive efficacy and safety, including short- and long-term side effects, and also return to fertility after removal.¹

It has been suggested that the contraceptive efficacy of copper IUDs correlates positively to the area of copper-releasing surface. However in the case of the Multiload IUDs, when the Multiload®Cu250 was compared to the Multiload®Cu375^{2,3} (Table 1), the latter had the highest pregnancy rates. Furthermore, Rhemrev et al⁴ compared the Multiload®Cu250, Multiload®Cu375 and MultiloadAgCu250 and concluded that the pregnancy rates showed no statistically significant differences. On the other hand, Rowe⁵ reviewed the pregnancy rates of four studies of the TCu220 compared to four studies of the TCu380 and found the pregnancy rates of the TCu380 to be lower in all but one of the studies. Therefore the evidence is conflicting as to whether the surface area of copper influences pregnancy rates.

Table 1 The Multiload IUD: Copper surface area and pregnancy rates

Study	Country	Device	N	Pregnancy rate at 12 months
McCarthy (1987) ²	Singapore	ML250	400	0.9 (net)
Bratt (1988) ³	Norway	ML250	200	0.5 (gross)
Bratt (1988) ³	Norway	ML375	198	1.1 (gross)

The Nova-T® IUD (also available as the Novagard® till May 1998) has been in extensive use in the UK for 16 years. It has a copper wire on the central stem with a surface area of 200 mm². Replacement is recommended after 5 years. The present study is of the Nova-T®380, in which the surface area of copper has been increased to 380 mm², all the copper being on the central stem. This IUD became available in the UK in 1999. A study of the Nova-T®380 device has been reported from Hungary and Finland⁶ the results of which are shown in Table 2.

The purpose of the study was to evaluate the pregnancy and complication rates of this new device, with its increased area of copper, in comparison with other published results, in the clinical setting of British general practice and family planning clinics.

Table 2 Nova-T®380, Nova-T® and GynaeT®380 Slimline: cumulative gross closure rates per 100 users

Study	Country	Device	N	Duration	Pregnancy	Pain/bleeding	Expulsion
Present study	UK	Nova-T®380	572	12 months	0.8	11.0*	5.6
Batar et al (1999) ⁶	Hungary	Nova-T®380	400	12 months	0.5	Bleeding 4.7,Pain 1.3	1.6
Batar et al (1999) ⁶	Finland	Nova-T®380	400	24 months	1.6	Bleeding 8.7,Pain 2.3	2.8
	Hungary						
UK Family Planning Research Network(1989) ⁸	UK	Nova-T®	438	12 months	0.0	5.4	4.4
Bratt (1988) ³	Norway	Nova-T®	200	12 months	0.6	6.1	4.3
Andersson(1994) ⁹	Sweden	Nova-T®	937	12 months	0.9	7.3	3.4 (net)
	Scandinavia						
deCastro(1987) ¹⁰	Hungary	Nova-T®	1116	12 months	1.8	1.8	3.5
Sivin et al (1993) ¹⁴	Spain	Nova-T®	419	12 months	0.3	7.7	5.9
	USA	GynaeT®380 Slimline	419	4 years	0.3	20.6	8.5
Sivin et al (1993) ¹⁴	USA	GynaeT®380 Slimline					

*combined rate for the 2 categories of removal for ‘bleeding problems’ and ‘bleeding and pain’ (Table 6).

Method

The study is an ongoing, open, single group, multicentre phase III study in out-patients. Doctors working in general practice and at family planning clinics throughout the UK who collaborate in the UK Family Planning and Reproductive Health Research Network were responsible for the Nova-T®380 fittings reported in this paper. The study is sponsored by Leiras Oy and Schering Health Care Limited. Ethics committee approval for the study was obtained at all centres.

The Nova-T®380 has a polyethylene frame shaped as a modified T with 380 mm² of silver-cored copper wound round the vertical arm. The silver core is intended to prevent corrosion-induced fragmentation.

The device was fitted according to the doctor’s own clinical judgement, in parous women attending for family planning advice and requesting intra-uterine contraception. Those enrolled were parous women aged 18-45, exposed to the risk of pregnancy, in good health and with normal menstrual cycles. They were fitted with their IUD more than 6 weeks after pregnancy ended. After entry to the study, the subjects are being followed for 5 years.

After insertion of the IUD, each subject was requested to return for follow-up examination at 3 months, 12 months and annually thereafter. Baseline data and details of the fitting procedure and follow-up visits were forwarded to the Institute of Population Studies, School of Postgraduate Medicine and Health Sciences, Exeter University, where the data was processed and analysed. Event rates were calculated using the life table method.⁷ Adverse events were classified using the WHO Adverse Reaction Dictionary (version 1/1995). A programme of comprehensive monitoring using EU GCP Guidelines is being used. At the close of recruitment, 572 women had been recruited who satisfied the criteria of the study protocol. This paper concentrates on data from this per protocol sample for the first 12 months of use.

Results

Demographic characteristics

The age distribution is shown in Table 3. The mean age of the study population was 33 years (range 18-45 years). All the women were parous: 73.8% had given birth to one or two children and 29.2% had given birth to three or more children.

Table 3 Age distribution

Age group	Number	Percent
18–24	55	9
25–29	149	26
30–34	140	25
35–39	146	26
40–45	80	14
Total	570	100

2 missing observations

Contraception prior to fitting

The contraceptive method used prior to fitting is shown in Table 4. Previous IUD users are likely to have a relatively good result with a new IUD.

Table 4 Contraceptive method used prior to study IUD fitting

Method	Number	Percent
IUD	166	29
Oral contraception	132	23
Injectable	8	1
Condom	183	32
Cap/diaphragm	12	2
Rhythm/withdrawal	6	1
Spermicide	1	0.2
More than one	7	1
Other	7	1
None	39	7
Unknown	11	2
Total	572	100

Fitting experiences

Investigators reported 33 (6%) fittings as ‘difficult’. Forty-one (7%) fittings needed dilatation of the cervix; seven of the 41 were described as ‘difficult’ by the investigator. Fitting was comfortable for most study subjects, with 84% experiencing no pain or only mild pain (Table 5). The numbers offered or given analgesia or local anaesthesia are not known.

Life table closure rates.

The cumulative gross rates for closure of study at 3 and 12 months are given in Table 6. These show the Nova-T®380 IUD to have a low pregnancy and a moderate expulsion rate. The continuation rate at 12 months for the study population was 73.4.

Table 5 Pain at insertion

	Number	Percent
Severe	7	1
Moderate	84	15
Mild	261	46
None	216	38
Total	568	100

4 missing observations

Pregnancy

The cumulative gross rate for pregnancy was 0.6 (confidence interval (CI) 0.1-1.7) at 3 months and 0.8 (CI 0.2-2.1) at 12 months (Table 6). Four pregnancies occurred during the first 12 months, of which two were ectopic and two were terminated.

Case report 1. There had been no menstrual bleeding since insertion. An ultrasound at 2 months use showed a 7 week gestation with the IUD lying in the cervical part of the uterus. The IUD was removed and the pregnancy terminated.

Case report 2. A visit at 5 months reported no missed periods. At 6.5 months of use an ectopic pregnancy occurred. The IUD was removed from the uterus and the ectopic pregnancy was removed by laparotomy.

Case report 3. Attended the clinic 6 months after insertion complaining of heavy bleeding for 16 days. Re-attended 5 days later when a pregnancy test was positive and the IUD was found to be partially expelled. On ultrasound a twin pregnancy was seen. The IUD was removed and the subject intended to terminate the pregnancy. Admitted to hospital 3 weeks later with a threatened abortion. An induced abortion was performed. The duration of pregnancy was estimated to be 7 weeks.

Case report 4. Admitted to hospital at 3.5 months of use. An ectopic pregnancy was diagnosed and a right salpingectomy performed. The IUD was removed from the uterus. Duration of pregnancy estimated to be 11 weeks.

Removal following a complaint of bleeding and bleeding with pain

A total of 46 women had the device removed at or before 12 months of use following a complaint of bleeding problems or bleeding and pain (Table 6). The average length of use before removal of the device for these reasons at 12 months of use was 6.4 months. The types of bleeding problems are shown in Table 7. Data on methods of treating bleeding or pain was not collected systematically.

Table 6 Cumulative life-table gross closure rates per 100 users at 3 and 12 months (per protocol sample of 572)

	N	3 Months Gross rate	CI	N	12 Months Gross rate	CI
Pregnancy	3	0.6	0.1-1.7	4	0.8	0.2-2.1
Expulsion	21	3.9	2.2-5.6	28	5.6	3.5-7.6
Bleeding problems	2	0.4	0.0-1.4	24	6.0	3.7-8.4
Pain	5	1.0	0.3-2.3	8	1.9	0.8-3.7
Bleeding and pain	6	1.1	0.4-2.4	22	5.3	3.1-7.4
Perforation	0	0.0	0.0-0.0	0	0.0	0.0-0.0
PID	0	0.0	0.0-0.3	4	1.0	0.3-2.6
Other complaint associated with IUD	2	0.4	0.0-1.3	7	1.8	0.7-3.7
Planning pregnancy	2	0.4	0.1-1.6	16	4.4	2.3-6.6
Other reason	2	0.4	0.0-1.4	12	3.1	1.4-4.9
Medical problem not related to IUD use	0	0.0	0.0-0.3	1	0.3	0.0-1.8
Total discontinuations	43	8.0		126	26.6	
Continuation		92.0			73.4	

Table 7 Bleeding problems leading to removal at or before 12 months of use

Reason for removal	Number	Percent
Heavier periods/'bleeding'	29	63
Continuous/persistent vaginal loss	14	30
Oligomenorrhoea	2	4
Other	1	2
Total	46	100

Other medical complaints requiring removal

The rate for removals for 'other complaints associated with IUD use' (Table 6) was 0.4 (n = 2) at 3 months and 1.8 (n = 7) at 12 months. Within this category, male dyspareunia was a contributory complaint in four cases. Other complaints included stomach cramps, candida, vaginal irritation, water retention, and offensive discharge.

Pelvic inflammatory disease

The diagnosis depended on the judgement of the clinician involved. There were seven cases of PID, though the diagnosis was doubtful in one case (Table 8). In four of these cases the IUD was removed. The organisms responsible were not determined. All were treated successfully with antibiotics without admission to hospital. The relationship of PID to IUDs is uncertain and is discussed below.

Discussion

Table 2 shows the published results obtained with various devices. The 4 Nova-T® studies^{3,8-10} showed pregnancy rates of 0.6, 0.0, 0.9 and 1.8 at 12 months, respectively. The pregnancy rate in the present study of the Nova-T®380 of 0.8 shows no clear improvement. Neither does the pregnancy rate of 0.5 at 12 months obtained in the study by Batar et al⁶ show a clear improvement. The increased surface area of copper was not associated with a reduced pregnancy rate, but as this was not a direct comparative study with the Nova-T®, the influence of the increased area of copper must remain somewhat uncertain. As all pregnancy rates are low, it is not easy to produce any improvement with copper IUDs.

The diagnosis of PID depended on the clinical judgement of the clinician involved as laparoscopy was not used. The seven cases of PID, (one of them of uncertain diagnosis) could have been related to the IUD. However, the frequency of PID has been shown in recent studies to be only minimally, if at all, related to the copper IUD. Of greater significance is exposure to sexually transmitted infection rather than the presence of an IUD.¹¹ During the period of this study only some centres were carrying out screening and prophylactic measures for *Chlamydia* and other

Table 8 Pelvic inflammatory disease

Age	Duration of IUD use	Severity	Investigation/Treatment	IUD removed	Result
32	1 month	moderate	Augmentin®, Metronidazole	No	Cured
32	9 months	mild	Amoxycillin, Metronidazole	No	Cured
37	4 months	moderate	Oxytetracycline	Yes	Cured
29	7 months	mild	Penicillin	Yes	Cured
40	6.5 months	mild	Doxycycline, Metronidazole	No	Cured
20	4 months	moderate	Two episodes, Antibiotics	Yes at 2nd episode	Cured
*21	6 months	—	Treated as hospital outpatient	Yes	Cured

* diagnosis doubtful as little information available from GUM clinic which treated her.

organisms. There appeared to be no increased risk of PID soon after fitting as has been reported elsewhere.¹²

The discontinuation rates for bleeding problems and pain with bleeding in the present study were higher than in the paper by Baxter et al.⁶ Other event rates were consistent with other published studies. It is of interest to compare this to the rate of 5.4 in the study of the Nova T[®] carried out in very similar circumstances on a similar population, and with many of the same investigators⁸ (Table 2). There is no obvious explanation for the difference. Is it possible that with the passage of a decade British women have become less tolerant of bleeding/pain problems? Can the extra copper be blamed? A randomised comparison of the Multiload[®]Cu250 and the Multiload[®]Cu375³ showed the removal rate for pain/bleeding at 12 months to be 3.6 and 9.6, respectively, the difference being statistically significant. On the other hand, WHO studies¹³ showed very similar removal rates for the TCu220C and the TCu380A.

It is interesting to compare the Nova-T380[®] to the Ortho Gynae-T[®] Slimline, now discontinued in the UK, though it had been licensed for use up to 10 years. Table 2 gives the results at 12 months and at 4 years of one large study of the Slimline.¹⁴ The latter has very low pregnancy rates at 12 months and at 4 years. Expulsion and removal for pain/bleeding at 12 months are not vastly different from the present study. The main design difference in the two devices is that in the Nova-T380[®] the copper is entirely on the central stem whereas in the Slimline there is copper on the transverse arms and on the central stem. Could this difference be of any significance? Sivin et al¹⁴ have speculated that the placement of copper near the oviducts (as with the Slimline) enhances contraception.

Conclusion

In this study, increasing the surface area of copper did not seem to be associated with a reduced pregnancy rate, but as

this was not a direct comparative study with the Nova-T[®], the influence of the increased area of copper must remain somewhat uncertain. There was a very low pregnancy rate. There was a higher than expected removal for pain bleeding. Other complications were similar to other published studies.

Acknowledgements

The Nova-T[®]380 IUDs were supplied by Leiras Oy. Statistical analysis by Ruth Preist, Hilary Hardwicke and Sarah Blacksell of the Institute of Population Studies, University of Exeter. Supervision by Dr John Tripp of the School of Postgraduate Medicine and Health Sciences, University of Exeter.

Statements on funding and competing interests

Funding. This study is sponsored by Leiras Oy and Schering Health Care Limited.
Competing interests. None.

References

1 World Health Organisation. Mechanism of action, safety and efficacy of intrauterine devices. Technical Report Series 753. Geneva: WHO, 1987.
2 McCarthy T, Ramachandran L, Ratnam SS. Interim 4-year results of a comparative study between the Nova T and the Multiload 250. *Adv Contracept* 1987; **3**: 323–326.
3 Bratt H, Skjeldestad FE, Valentin KC. A randomised trial of three Copper IUDs. *Acta Obstet Gynecol Scand* 1988; **67**: 247–251.
4 Rhemrev PER, Van Os WAA, et al. Comparison of three Multiload IUDs: MLCu250, MLCu375 and MLCu380. *Adv Contracept* 1985; **1**: 31–36.
5 Rowe PJ. Clinical Performance of Copper IUDs. *Proceedings from the Fourth International Conference on IUDs*. Bardin CW, Mishell JrDR (eds). Boston, Mass: Butterworth-Heinemann 1994: Chapter 2, 13–29.
6 Batár I, Kuukankorpi A, et al. Two-year clinical experience with Nova-T 380, a novel copper-silver IUD. *Adv Contracept* 1999; **15**: 37–48.
7 Tietze C, Lewitt S. Recommended procedures for the statistical evaluation of intrauterine contraception. *Studies in Family Planning* 1973; **4** (No 2): 35–42.
8 UK Family Planning Research Network. A multicentre use-effectiveness study of the Novagard intrauterine device. *Br J Family Planning* 1989; **15**: 36–37.
9 Andersson K, Odland V, Rybo G. Levonorgestrel-releasing and copper-releasing (NovaT) IUDs during five years of use. *Contraception* 1994; **49**: 56–72.
10 deCastro A, Perez-Iglesias R, et al. Comparison of two copper IUDs: the MLCu375 and the Nova-T. *Adv Contracept* 1987; **3**: 319–322.
11 Bromham DR. Intrauterine contraceptive devices- a reappraisal *Br Med Bull* 1993; **49**:100–123.
12 Farley TMH, Rosenberg MJ, Rowe P. Intrauterine devices and pelvic inflammatory disease: an international perspective. *Lancet* 1992; **339**: 785–788.
13 World Health Organisation Special Programme of Research in Human Reproduction. The TCu380A, TCu220C, Multiload 250 and NovaT IUDs at 3.5, and 7 years of use- results from three randomised multicentre trials. *Contraception* 1990; **42**: 141–148.
14 Sivin I, Diaz J, et al. Four-year experience in a randomised study of the Gyne T[®]380 Slimline and the standard Gyne T[®]380 intrauterine copper devices. *Contraception* 1993; **47**: 37–42.

Corrections

In the January 2000 issue (Volume 26, Number 1) the Journal citations given at the top of pages 39, 44 and 52 were mistakenly given as 1999 rather than 2000. The correct references for the relevant papers are as follows:

Latthe M, Latthe PM, Charlton R. Quality of information on emergency contraception on the Internet. *Br J Fam Plann* 2000; **26** (1): 39–43.

Edouard L, Olatunbosun O. Sexual and reproductive rights: statements, rhetoric and responsibilities. *Br J Fam Plann* 2000; **26** (1): 44–47.

Bigrigg A, Evans M, Gbolade BA, et al. Depo Provera discussion paper on clinical care, effectiveness and side effects. *Br J Fam Plann* 2000; **26** (1): 52–53.

In the FACT Review published in the April 2000 issue (Elliman A. Interactions with hormonal contraception. *Br J Fam Plann* 2000; **26** (2): 109–111), reference 11 should have been printed as follows:

Chesne C, Kanmacher I, Benel L, et al. Effects of modafinil on cytochrome-P450-dependent enzyme activities in cultured human hepatocytes. *14th Eur Workshop Drug Metab (July 3–9, Paris)* 1994: Abstract B23.

In the Guidance April 2000 Emergency Contraception: Recommendations for Clinical Practice, LevonelleTM-2 is the correct name and not Levonelle[®]-2.

We apologise for any confusion these errors may have caused.