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META-ANALYSIS *Gynaecology*

The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience

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BACKGROUND: Intrauterine devices (IUDs) have been studied for use for emergency contraception for at least 35 years. IUDs are safe and highly effective for emergency contraception and regular contraception, and are extremely cost-effective as an ongoing method. The objective of this study was to evaluate the existing data to estimate the efficacy of IUDs for emergency contraception.

METHODS: The reference list for this study was generated from hand searching the reference lists of relevant articles and our own article archives, and electronic searches of several databases: Medline, Global Health, Clinicaltrials.gov, Popline, Wanfang Data (Chinese) and Weipu Data (Chinese). We included studies published in English or Chinese, with a defined population of women who presented for emergency contraception and were provided with an IUD, and in which the number of pregnancies was ascertained and loss to follow-up was clearly defined. Data from each article were abstracted independently by two reviewers.

RESULTS: The 42 studies (of 274 retrieved) that met our inclusion criteria were conducted in six countries between 1979 and 2011 and included eight different types of IUD and 7034 women. The maximum timeframe from intercourse to insertion of the IUD ranged from 2 days to 10 or more days; the majority of insertions (74% of studies) occurred within 5 days of intercourse. The pregnancy rate (excluding one outlier study) was 0.09%.

CONCLUSIONS: IUDs are a highly effective method of contraception after unprotected intercourse. Because they are safe for the majority of women, highly effective and cost-effective when left in place as ongoing contraception, whenever clinically feasible IUDs should be included in the range of emergency contraception options offered to patients presenting after unprotected intercourse. This review is limited by the fact that the original studies did not provide sufficient data on the delay between intercourse and insertion of the IUD, parity, cycle day of intercourse or IUD type to allow analysis by any of these variables.

Key words: emergency contraception / intrauterine device / unintended pregnancy / unprotected intercourse / contraception

Introduction

Unintended pregnancy is a significant problem worldwide. It is estimated that globally at least 36% of pregnancies are unintended (Singh *et al.*, 2009), and in the USA nearly half of pregnancies are unintended (Finer and Zolna, 2011). Emergency contraception offers women an important strategy to prevent pregnancy after intercourse in cases of contraceptive accidents or non-use, or in situations of sexual violence. There are two forms of emergency contraception available today: pills and intrauterine devices (IUDs). The most common medication option is 1.5 mg levonorgestrel, sold in one-pill or two-pill formulations. A newer formulation is 30 mg ulipristal acetate, marketed in the USA as ella® and in much of Europe as ellaOne®. In a few places, such as China, Vietnam and Russia, mifepristone in small doses is available for emergency contraception.

Non-hormonal IUDs (primarily copper-bearing) have been used for emergency contraception for at least 35 years (Lippes *et al.*, 1976). (The levonorgestrel intrauterine system, sold in the USA and Europe under the brand name Mirena®, has not been studied for use for emergency contraception.) Negative experiences with the Dalkon

Shield, an IUD available in the 1970s in the USA, led to years of concern about the safety of IUDs and very low levels of IUD use. However, the design of modern IUDs available today is vastly improved, and guidelines from major medical organizations, such as the Centers for Disease Control and Prevention, the World Health Organization, the UK Faculty of Sexual and Reproductive Healthcare and American College of Obstetricians and Gynecologists, note that IUDs are a safe choice for the majority of patients, including young and nulliparous women (World Health Organization, 2009; ACOG Practice Bulletin, 2010; Centers for Disease Control and Prevention, 2010; Faculty of Sexual & Reproductive Healthcare, Clinical Effectiveness Unit, 2011).

One of the major advantages of copper IUDs is that following use for emergency contraception, they can then be left in place to provide at least 10 years of highly effective ongoing contraception. [In the USA ParaGard® is labeled for 10 years of use but there is evidence of efficacy with longer use (Dean and Schwarz, 2011).] IUDs have been shown to be among the most cost-effective methods of contraception (Trussell *et al*., 2009); the fact that this is a 'forgettable' method that does not require action on the part of the user means that there is virtually no scope for user error.

IUDs are experiencing a moderate comeback after years of very low uptake in the USA (Hubacher *et al*., 2011). In 2008 (the last year for which data are available), 4.9% of American women at risk of pregnancy reported using an IUD (Mosher and Jones, 2010). This is a marked increase from the 0.7% of women at risk of pregnancy choosing IUDs in 1995 (Mosher and Jones, 2010) but is still lower than the use in Europe, where 10% of British women (data from 2009) (Lader, 2009) and 24% of French women (data from 2005) (Moreau *et al*., 2008) at risk of pregnancy use IUDs. No comparable statistic is available for IUD use among all women at risk of pregnancy in China, but the Chinese National Population and Family Planning Commission reported that 53% of married women using contraception used IUDs in 2009 (National Population and Family Planning Commission, Population and Development Research Center of China, 2010). IUD use is higher in China than in the world overall; a 2005 report noted that 43% of Chinese women using contraception used IUDs, compared with 13% in the rest of the world (Salem, 2006). Guidelines for the use of IUDs for emergency contraception typically recommend inserting the IUD within 5 days of unprotected intercourse (ACOG Practice Bulletin, 2010), although the Centers for Disease Control, the World Health Organization and the UK Faculty of Sexual and Reproductive Healthcare specify that an IUD can be used beyond 5 days, as long as the time of ovulation can be reasonably determined and the insertion occurs no more than 5 days after ovulation (World Health Organization, 2009; Centers for Disease Control and Prevention, 2010; Faculty of Sexual & Reproductive Healthcare, Clinical Effectiveness Unit, 2011). It should be noted that the guidelines around the time of insertion are not related to efficacy or safety but to ensure that the IUD is inserted before the implantation of an embryo (thus ensuring its function as a contraceptive, rather than an early abortifacient).

Materials and Methods

This study is a systematic review designed to provide a current estimate of the efficacy of IUDs used for emergency contraception, based on all of the available published data. The reference list for this study was generated from searching our own archives, references lists of relevant articles and queries of several databases using the following search terms:

MEDLINE: 'Contraception, Postcoital' [Mesh] AND 'Intrauterine Devices' [Mesh],
Clinicaltrials.gov: 'intrauterine device' AND 'emergency contraception',
Popline: 'IUD' & 'Emergency Contraception',
Global Health: 'intrauterine device' AND 'emergency contracept*' OR 'postcoit* contracept*',
Wanfang Data (Chinese): (emergency contraception, intrauterine device),
Weipu Data (Chinese): (emergency contraception, intrauterine device).

This review includes any peer-reviewed study published by August 2011 in English or Chinese, with a defined population of women who presented for emergency contraception and were provided with an IUD, and in which the number of pregnancies was ascertained and loss to follow-up was clearly defined. Chinese data were included because of the tremendous amount of contraceptive research taking place in that country.

Once relevant articles were identified, data from each study were abstracted independently by two reviewers using a common data entry form that captured the language of publication, country in which data were collected, type(s) of IUD used, maximum time from intercourse to IUD insertion, initial study enrollment, efficacy-evaluable population, loss to follow-up and number of treatment failures (pregnancies).

We computed Blyth–Still–Casella exact 95% binomial confidence intervals (CI) for proportions and used either Fisher's Exact Test (for 2×2) or Fisher–Freeman–Halton (for $R \times 2$) to test for homogeneity. All calculations were performed in StatXact in Cytel Studio 8 (Cytel Inc., Cambridge, MA, USA).

Results

Our search found 274 articles, and we assessed 48 of these in depth to determine their eligibility for inclusion. Five studies were excluded from our analysis because they did not provide sufficient detail about the loss to follow-up (Bromwich and Parsons, 1982; Hutchinson, 1983; Wright and Thompson, 1986; Friedman and Rowley, 1987; Zhang and Huang, 2005). In addition, one study was published both in English and Chinese, and we included the English version in this analysis (Fan and Zhou, 2001; Zhou and Xiao, 2001). This study included a subject who presented 95 h after unprotected intercourse and was believed to be pregnant as a result of an act of intercourse 16 days prior to insertion of the IUD; this individual was excluded from the analysis. One study was designed to compare the insertion tolerability of the GyneFix IUD versus the Gyne-T380S IUD for emergency contraception but it did report that no pregnancies occurred in the trial, and so we included it in our final dataset (D'Souza *et al*., 2003). Forty-two studies were included in the final review.

The 42 studies that fit our eligibility criteria and were included in the review ranged in the year of publication from 1979 to 2011 (Table I). Of these, 28 were published in Chinese and 14 in English. The English literature included data collected in China, Egypt, Italy, the Netherlands, USA and the UK. Nearly all of the IUDs were copper-bearing, although a small number of plastic IUDs (the Lippes Loop series) were used in two of the earlier studies (Black *et al*., 1980; Guillebaud *et al*., 1983). The majority of studies in our review (31 studies, 74%) followed the current standard protocol of inserting the IUD within 5

Table I Studies included in review of the efficacy of IUDs for emergency contraception over 35 years, in order of publication.

Study	Country	IUD type	Max. time to insertion (days)	Enrolled (*n*)	Efficacy population (*n*)	Pregnancies (*n*)	Pregnancy rate (%) (95% CI)[a]
Gottardi *et al.* (1979)[b]	Italy	Cu T-200	2	60	60	0	0 (0–6.0)
Lippes *et al.* (1979)[b]	USA	Cu T-200, Cu 7	7	299	299	0	0 (0–1.2)
Tyrer (1980)[b]	USA	Cu 7	5	80	80	0	0 (0–4.5)
Black *et al.* (1980)[b]	UK	Cu 7, Lippes Loop D	10	191	176	0	0 (0–2.1)
Van Santen and Haspels (1981)[b]	Netherlands	MLCu-250, Cu 7, Cu T-200	5	55	55	0	0 (0–6.5)
Goldstuck (1983)[b]	UK	Cu 7, Cu 7 Mini, Cu T, MLCu 250, MLCu 250 short	10+	71	64	0	0 (0–5.6)
Guillebaud *et al.* (1983)[b]	UK	Cu 7, Lippes Loop	5	87	87	0	0 (0–4.2)
Gottardi *et al.* (1986)[b]	Italy	Cu T-200, Cu 7, Cu 7 Mini, MLCu-250	7	98	91	0	0 (0–4.0)
Luerti *et al.* (1986)[b]	Italy	MLCu-250, Cu 7, Cu T	7	117	102	0	0 (0–3.6)
Askalani *et al.* (1987)[b]	Egypt	Cu T-200	4	200	200	4	2.0 (0.5–5.0)
Yang *et al.* (1997)	China	ML Cu-375 SL	5	30	30	0	0 (0–11.6)
Li *et al.* (1999)	China	ML Cu-375 SL	5	101	101	0	0 (0–3.6)
Zhang *et al.* (1999)	China	ML Cu-375 SL	5	100	100	0	0 (0–3.6)
Lu (2000)	China	Copper IUD (unspecified)	5	28	28	0	0 (0–12.3)
Tian (2000)	China	Copper IUD (unspecified)	5	80	80	0	0 (0–4.5)
Li *et al.* (2001)	China	Cu T-380A	5	94	94	0	0 (0–3.8)
Zhao *et al.* (2001)	China	ML Cu-375 SL	5	98	98	1	1.0 (0.0–5.6)
Zhou and Xiao (2001)[b]	China	ML Cu-375 SL	5+	1013	998	1	0.1 (0.0–0.6)
Liu and Chen (2002a,b)	China	ML Cu-375 SL	5	80	80	1	1.2 (0.0–6.8)
Liu and Chen (2002a,b)	China	Copper IUD (unspecified)	3	95	95	0	0 (0–3.8)
Sun *et al.* (2003)	China	GyneFix	5	86	86	0	0 (0–4.2)
D'Souza *et al.* (2003)b	UK	GyneFix, Gyne-T 380S	Unspecified	173	169	0	0 (0–2.2)
Tang *et al.* (2003)	China	ML Cu-375 SL	5	98	98	1	1.0 (0.0–5.6)
Wang and Jiang (2003)	China	Copper IUD (unspecified)	5	86	86	0	0 (0–4.2)
Zhao and Wang (2004)	China	Cu T-220	5	108	108	0	0 (0–3.4)
Hou (2005)	China	Nova T-380	5	100	100	0	0 (0–3.6)
Li *et al.* (2005)	China	ML Cu-375 SL	5	150	150	0	0 (0–2.4)
Wen (2005)	China	Cu T-380A	5	218	218	1	0.5 (0.0–2.5)

Continued

Table I *Continued*

Study	Country	IUD type	Max. time to insertion (days)	Enrolled (*n*)	Efficacy population (*n*)	Pregnancies (*n*)	Pregnancy rate (%) (95% CI)[a]
Wang *et al.* (2006)	China	Cu T-380A	5	200	200	0	0 (0–1.8)
Dong and Wu (2007)	China	Copper IUD (unspecified)	5	87	87	0	0 (0–4.2)
Sheng and Zhang (2007)	China	Copper IUD (unspecified)	5	27	27	0	0 (0–12.8)
Song *et al.* (2007)	China	ML Cu-375 SL	5	180	180	0	0 (0–2.0)
Yang *et al.* (2008)	China	Cu T-380A	5	100	100	0	0 (0–3.6)
Hong (2008)	China	GyneFix	5	100	100	0	0 (0–3.6)
Ma *et al.* (2008)	China	MCu	5	26	26	0	0 (0–13.2)
Yang *et al.* (2008)	China	ML Cu-375 SL	5	86	86	0	0 (0–4.2)
He (2009)	China	Copper IUD (unspecified), ML Cu-375 SL	5	108	108	0	0 (0–3.3)
Hong (2009)	China	Copper IUD (unspecified)	5	70	70	0	0 (0–5.1)
Liu *et al.* (2010)	China	ML Cu-375 SL	5	162	162	1	0.6 (0.0–3.4)
Turok *et al.* (2010)[b]	USA	Cu T-380A	5	23	22	0	0 (0–15.4)
Wang (2010)	China	Copper IUD (unspecified)	5	40	40	0	0 (0–8.8)
Wu *et al.* (2010)[b]	China	Cu T-380A	5	1963	1893	0	0 (0–0.2)

[a]Where the pregnancy rate is zero, a one-sided 97.5% CI is calculated. Otherwise, a 95% exact binomial CI is calculated.
[b]Indicates publication in English; otherwise, studies were published in Chinese.

days of unprotected intercourse, although one study included 18 (out of 998) insertions beyond 5 days (Zhou and Xiao, 2001), three studies provided insertions up to 7 days after intercourse (Gottardi *et al.*, 1979; Lippes *et al.*, 1979; Luerti *et al.*, 1986), one allowed insertions up to 10 days (Black *et al.*, 1980) and one included 24 insertions (out of 64) at 10 or more days post-coitus (Goldstuck, 1983). One study did not specify the time to insertion at all (D'Souza *et al.*, 2003). The studies did not include sufficient information on the delay between intercourse and insertion of the IUD to enable us to analyze the data by delay.

Among 7034 post-coital IUD insertions, there were 10 pregnancies, for an overall failure rate of 0.14% (95% CI = 0.08–0.25%) (Table II). Six pregnancies occurred among 5629 subjects in the studies conducted in China (failure rate = 0.11%; 95% CI = 0.05–0.23%) and the remaining four pregnancies occurred among 200 subjects in one study conducted in Egypt (Askalani *et al.*, 1987). Strikingly, this study is the only RCT with a non-treatment arm for a contraceptive product that we are aware of. Three hundred women who had engaged in unprotected intercourse around the time of ovulation (and so had a relatively high probability of pregnancy) were randomized to either post-coital insertion of a Cu T-200 or no treatment. The pregnancy rates were 2% among the treatment group and 22% in the expectant management group. The failure rate in the treatment arm of this study is surprisingly high, and significantly higher than the rate in all other countries combined ($P = 0.0001$); in contrast, the results among the five countries excluding Egypt are homogeneous ($P = 1$). If the true failure rate in Egypt were the same as in the other five countries (0.000878), then the chance of observing four or more pregnancies is vanishingly small, ~1 in 30 000 ($P = 0.00004$). This high failure rate can possibly be explained by the fact that women were specifically selected if they had had intercourse around the time of ovulation; in any event Egypt is a clear outlier. If the unusual results from the Egypt study were excluded, the overall failure rate would be 0.09% (95% CI = 0.04–0.19%); this is our preferred estimate.

Discussion

Our data suggest that IUDs are a highly effective method of emergency contraception, with a failure rate of less than one per thousand. The copper IUD is by far the most effective emergency contraceptive option, followed by mid-dose mifepristone (25–50 mg) or ulipristal acetate (failure rate ~1.4%) and then levonorgestrel (failure rate ~2–3%) (Cheng *et al.*, 2008; Glasier *et al.*, 2010).

Table II Failure rates for IUD use as emergency contraception, by country.

Country	Population	Pregnancies	Rate (%)	Exact 95% CI (%)	
China	5629	6	0.11	0.05	0.23
UK	496	0	0.00	0.00	0.70
USA	401	0	0.00	0.00	0.85
Italy	253	0	0.00	0.00	1.38
Egypt	200	4	2.00	0.69	5.03
The Netherlands	55	0	0.00	0.00	5.93
Total	7034	10	0.14	0.08	0.25
Total excluding Egypt	6834	6	0.09	0.04	0.19

Data from two randomized trials of the ulipristal acetate and levonorgestrel regimens suggest that the efficacy of levonorgestrel declines sharply as BMI increases. Statistical models indicate that, among women with a BMI of 26 kg/m^2 or higher presenting after unprotected intercourse, levonorgestrel is no more effective than no treatment. Ulipristal acetate appears to retain its efficacy at higher BMI levels but is no more effective than no treatment at a BMI of 35 or higher (Glasier *et al.*, 2011). There is no clinical concern about the loss of effectiveness of the IUD with an increase in BMI; therefore, an IUD would be a particularly good choice for obese women presenting after unprotected sex.

Several recent studies exploring the awareness of and the interest in IUDs among women seeking emergency contraception identified barriers to a greater use of IUDs including cost, waiting time (patients are not always able to get an IUD the day that they present for emergency contraception), low levels of awareness and understanding among patients and lack of participation among providers (Schwarz *et al.*, 2009; Bharadwaj *et al.*, 2011; Turok *et al.*, 2011; Wright *et al.*, 2012). Two of these studies found that around 12% of women presenting for emergency contraception or walk-in pregnancy testing would consider an IUD as an alternative to emergency contraceptive pills (Schwarz *et al.*, 2009; Turok *et al.*, 2011); this finding indicates the considerable potential to increase IUD uptake among women who have recently had unprotected sex. A study of contraceptive providers in CA, USA, showed that 85% of clinicians never recommended the IUD for emergency contraception, and 93% require at least two visits for an IUD insertion (Harper *et al.*, 2012).

Our review has several limitations. The initial intention of this study was to assess the efficacy of IUDs for emergency contraception by the day of insertion (how many days had elapsed between unprotected intercourse and insertion of the IUD), but the studies generally did not include sufficient detail about the day of insertion among the efficacy-evaluable population. Therefore, our analysis groups all cases together, regardless of the length of delay between intercourse and insertion of the IUD. Similarly, we are unable to provide estimates of the efficacy by parity, individual pregnancy risk (the cycle day on which intercourse occurred) and IUD type, as most studies did not provide detailed information on these variables. Finally, as in any review, it is possible that studies may have been unintentionally excluded owing to incomplete search results. We were not able to include publications in languages other than English and Chinese; it is a limitation that relevant studies in other languages were omitted, as these might have added strength to these results. However, we believe that English and Chinese journals include the majority of publications on this topic.

Conclusions

Despite the limitations of the original data, this study contributes to the literature and to clinical practice by providing the most comprehensive review to date of the efficacy of IUDs used for emergency contraception. These results provide clear evidence that IUDs are a highly effective method of emergency contraception, as 99.86% of users overall did not become pregnant after unprotected intercourse when an IUD was inserted post-coitally. When we exclude the data from the Egyptian study (which does not represent the typical clinical scenario because the investigators intentionally selected women who were at a greater risk of pregnancy), the failure rate is 0.09%.

The cost, clinical protocols and lack of awareness among both patients and providers are barriers to a greater uptake of IUDs for emergency contraception. Increasing the use of IUDs for emergency contraception is an important strategy for reducing an individual woman's chance of becoming pregnant after unprotected intercourse. In addition, if left in place for ongoing contraception, copper IUDs provide highly effective contraception for at least 10 years, and can contribute to decreasing unintended pregnancy rates over the long term. Therefore, we conclude that IUDs should be routinely included as an emergency contraceptive option whenever clinically feasible and appropriate.

Authors' roles

K.C. conducted the English literature search, abstracted data from the English literature and drafted the article. H.Z. conducted the Chinese literature search, abstracted data from the Chinese literature and provided comments on the manuscript. N.G. abstracted data from the English literature and provided comments on the manuscript. L.C. abstracted data from the Chinese literature and provided comments on the manuscript. J.T. oversaw the quantitative analysis and provided comments on the manuscript.

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Conflict of interest

None declared.

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