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The reliability of the anchoring concept for suspension of bioactive substances in the human uterus evaluated by measuring the removal force: results after long-term use

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Abstract

Objective: The objective of the present study is to report on the force needed to remove the implanted GyneFix® intrauterine contraceptive device (IUD) from the uterine cavity. This study is the first long-term study on the retrieval of the anchored IUD.
Study design: A two-center, noncomparative study to measure the force needed to remove the IUD in 251 women. A dynamometer (Pesola®, Switzerland) was used to measure the removal force in newtons.
Results: The results of this study show a mean removal force of 6.2 and 6.1 newtons, respectively (range, 0–10), in parous and nulligravid or nulliparous women ($p = 0.62$). There was no difference in removal force for those women with a duration of use either less than 60 months or longer than 60 months (median of 6 newtons in both groups; $p = 0.22$).
Conclusions: The force needed to remove the GyneFix IUD suggests that the implantation technology used in the insertion of the device is reliable, provided the anchoring knot is properly inserted in the fundal myometrium. The results of this study indicate that early expulsion of the device could be explained by failure to implant the knot adequately (no implantation or partial implantation), which requires a degree of skill. The present study does not provide an explanation for the occurrence of late expulsion, although some speculations can be made.

Keywords: "Frameless" intrauterine device (IUD); GyneFix®; Removal force; Failed insertion; Expulsion

1. Introduction

The "frameless" GyneFix® IUD was developed to maximize the contraceptive effect by suspending the active contraceptive substance, copper, in the upper part of the uterine cavity while minimizing the foreign-body interference with the endometrial cavity to reduce pain and expulsion of the device.

The currently available "frameless" intrauterine copper-releasing contraceptive devices are unlike conventional "framed" IUDs. They consist of a length of nonbiodegradable 00-size or 0-size monofilament surgical thread with a varying number of copper tubes mounted on it; six copper tubes for the standard GyneFix and four in the case of the mini-GyneFix. With each device, the upper and lower tubes are crimped onto the thread to keep the copper cylinders in place. The total surface area of copper with standard IUD is 330 mm^2 and 200 mm^2 with the mini version. The upper extremity of the thread ends in a knot that is implanted into the myometrium of the uterine fundus using a specially designed insertion instrument, thereby permanently securing the device in the uterine cavity, as described previously. The anchorage site has been studied histologically in hysterectomy specimens with a frameless IUD that had been inserted up to 4 years previously [1]. The maximum histological reaction observed was 0.5 mm around the anchoring knot (Sewell scoring system), thus demonstrating the safety and long-term compatibility of the anchoring system.

A review of 15 years of clinical experience has been published recently [2]. In randomized and nonrandomized clinical trials, expulsion rates have been variable. Long-term multicenter clinical trials using the current GyneFix insertion technique have shown low expulsion rates (which includes failed insertion) both in parous and nulliparous

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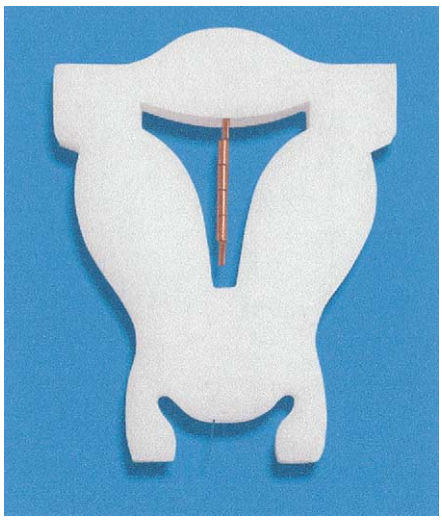

Fig. 1. The GyneFix® IUD in situ.

women ranging from 0.5 to 3.0% during the first 3 years of use, compared with expulsion rates of between 2.7 and 7.4% with the TCu380A IUD. However, in postmarketing trials, especially in the United Kingdom, expulsions have occurred in up to 8% during the first year [3–5]. Other centers in the United Kingdom did not report any expulsions [6,7].

The present study is an extension of previous, short-term studies in an attempt to find an explanation for early and late expulsion of the IUD and to provide recommendations for its prevention.

2. Materials and methods

2.1. Insertion of the GyneFix IUD

One-thousand and thirty-nine insertions were performed in this multicenter international study with an "improved" (Mark 1) applicator, as described previously [2]. The study was approved by the local ethics committees and informed consent was obtained within the multicenter trial. Women were followed-up at 1, 3, 6 and 12 months following insertion of the GyneFix IUD (Fig. 1) and every 6 months or yearly thereafter. At the end of the license period (5 years), the majority of GyneFix IUDs were removed in one center (Belgium) and the removal force was measured. In the Hungarian center, they were left in place (up to a maximum of 168 months) if the patient was problem-free and no pathological findings were detected at the routine follow-up visits.

2.2. Removal of the GyneFix IUD

To remove the GyneFix IUD, a hemostat was put on the tail of the device and the Pesola® dynamometer was hooked onto the hemostat. As the GyneFix IUD is retained in the uterus solely by the anchoring mechanism, the removal force was read at the precise moment when the anchor dislodged from the fundus of the uterus. The force was measured to the nearest integer. The removal force was compared between parous and nulliparous women and between two groups of women who had the device in place for <60 months or >60 months. Statistical analysis was carried out using analysis of variance for repeated measurements, with $p < 0.05$ denoting statistical significance [8].

Table 1
Removal force in women according to parity and duration of use

	Parity		No. of months in situ	
	0	>0	<60	>60
n	46	205	77	174
Mean	6.2	6.1	5.9	6.2
SD	1.9	2.2	2.3	2.1
Median	6.0	6.0	6.0	6.0
IQR[a]	4.5–8.0	4.5–7.5	4.0–8.0	4.5–7.5
Range	3–10	0–10	1.5–10	0–10
Mann–Whitney U-test	p = 0.62		p = 0.22	

[a] Interquartile range.

3. Results

The removal force, measured in newtons, was evaluated in 251 removals conducted in two centers, 117 in Hungary and 134 in Belgium. Table 1 shows the removal force in the total group of women and according to parity and duration of use (<60 months or >60 months). There were 46 nulligravid or nulliparous women and 205 parous women in the study. The median removal force was 6.0 and 6.0 newtons, respectively (range, 0–10), in parous and nulligravid or nulliparous women. In one case with IUD removal after 125 months, the removal force was 0. There was no statistically significant difference in the removal force either between the two groups of women according to parity ($p = 0.62$) or between the two groups of women with the device in situ for either less than 60 months or for longer than 60 months of use ($p = 0.22$).

4. Discussion

As most expulsions occur during the learning experience with GyneFix, it has been suggested that the skill of the physician performing the insertion is a major factor. Early expulsion is likely if the implantation of the anchor is not performed properly. The World Health Organization (WHO) has described the term "insertion failure" when applied to the GyneFix as the failure to implant the knot in the fundal myometrium. Failure to implant the knot means that the device stays in the uterine cavity but is not attached to the uterine wall as intended, resulting in the expulsion of the frameless IUD usually within days or weeks of the

attempted insertion. The fact that the majority of expulsions occur in a minority of doctors (6 of 28 centers accounted for 78% of insertion failures in the large WHO randomized clinical trial [9]) suggests that skill and experience played a part in failure to correctly insert the devices and this has been reported by other investigators [10–13].

The present study validates the concept of the anchoring principle and suggests that, when inserted correctly, spontaneous expulsion of the frameless IUD is unlikely. The force needed to remove the anchor from its position in the uterine wall is much higher than the force needed to remove a T-shaped IUD, which, for the standard TCu200 IUD, is between 1.0 and 1.7 newtons [14]. Early expulsion of the frameless IUD is, therefore, probably caused by improper anchoring, most likely due to lack of skill and experience.

The anchoring technique has been explained in detail previously [15]. An essential prerequisite to perform proper anchoring is to apply the inserter against the fundus prior to anchoring and not to move away from the fundus during the insertion procedure. To simplify the insertion procedure, a new applicator (Mark II inserter) has recently been introduced. With the Mark II, the anchoring is performed with one hand instead of two. Both Mark I and Mark II recommended insertion techniques can be viewed via the Internet [16].

The current GyneFix IUD has a 0-size knot, which has a more uniform size and is slightly bigger than the 00-size knot used in this removal study. This knot was selected because, in removal force studies, retention is stronger than with the 00-size knot.

5. Conclusion

The results of this study indicate that early expulsion of the device may be explained by failure to implant the knot adequately (no implantation or partial implantation), which requires a degree of skill. The present study does not provide an explanation for the occurrence of late expulsion. There is neither statistical difference in removal force between parous and nulliparous women, nor is there any indication that the anchoring is becoming less strong with time. Furthermore, spontaneous migration has not been detected in previous studies, which could explain the occurrence of late expulsions [17]. To minimize the risk of expulsion (early and late), it is recommended not to pull at the tail after insertion as the anchoring might still be weak, and to abstain from intercourse during the first week.

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“Conflict of Interest”: István Batár: nil. Dirk Wildemeersch is a Belgian gynecologist and Medical Director of Contrel Research, a company which was established to manage clinical research and to develop and study innovative drug technologies. Contrel is the manufacturer of GyneFix. The funds generated are reinvested in research.

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