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NOVEL METHOD AND DEVICE FOR DELIVERY AND RETENTION OF INTRAUTERINE DEVICES IN THE IMMEDIATE POSTPARTUM PERIOD: PILOT BABOON FEASIBILITY STUDY

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ABSTRACT

The immediate post-partum period offers a convenient time to have an intrauterine device placed because of the co-location of a non-pregnant woman and her clinician; however, this practice is associated with increased expulsion rates of up to 30%, compared with a 3% expulsion rate for interval insertions. This paper presents a device and method to improve intrauterine device delivery and retention in the immediate postpartum period. This initial feasibility study illustrates that it is possible to temporarily tether a commercially available intrauterine device within the uterus of an immediately postpartum baboon. The results indicate this device and method are technically feasible, but further studies will be needed to evaluate safety and efficacy in reducing expulsion rates.

Keywords: postpartum, intrauterine device, contraception, expulsion, unplanned pregnancy.

1. INTRODUCTION

Intrauterine devices (IUDs) placed in the immediate postpartum period (IPP) have higher expulsion rates, averaging 9% to 30% compared to the 3% expulsion rate of those placed as interval insertions. Interval insertions are performed before pregnancy or more than 6 weeks following delivery [1,2]. High IPP IUD expulsion rates seem to be influenced by a number of factors, including but not limited to changing geometries and contractile forces within the uterus during the puerperal period, clinician experience with the IPP IUD insertion procedure and fundal placement of the IUD [2-4]. The primary impact of expulsion is that the IUD's contraceptive effect is rendered ineffective, which sometimes results in unplanned pregnancies or short inter-pregnancy intervals (IPIs).

Research shows that short IPIs result in an increased risk of adverse pregnancy outcomes such as intrauterine growth restriction, spontaneous preterm deliveries, perinatal death, and poor maternal health such as preeclampsia and maternal depletion [5-7]. It is therefore imperative that effective contraception options are available and accessible to women, and the IPP period provides an ideal time for providing effective long acting reversible contraception because both the woman and provider are conveniently colocated.

Despite IUD effectiveness and low failure rates (0.2 – 0.6%) [8], IPP IUD insertion is underutilized, and up to 40% of women requesting intrauterine contraception are lost during the 6 week waiting period for interval insertions [9]. Recent studies have also suggested that IPP IUD insertion is not merely preferred, but practical, as its cost-effective nature for prevention of unplanned pregnancies exhibits an average cost savings ~$282,540 per 1000 women over a 2-year period [8].

Previous attempts have been made to retain IUDs in the IPP uterus to prevent premature expulsion, including IUDs to the fundal wall. Liu *et al* fixed IUDs to the IPP fundus following cesarean section using catgut, and reported 3% (n=130) expulsion at 42 days following the procedure [10]. More recently, permanently anchored IUDs have gained popularity in Europe and Asia: GyneFix® is a frameless copper IUD with a polypropylene suture threaded through copper sleeves. This IUD is permanently secured by inserting an anchoring knot in the fundal wall using a specially designed inserter. Unal *et al* anchored a frameless IUD –GyneFix® Cesarean Section IUD in an IPP uterus following a cesarean delivery, and reported a single expulsion (1.4%, n=70) [11]. Zhang *et al* inserted the GyneFix® PP IUD during cesarean

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section and reported 4% expulsion rate (n=200) [12]. The GyneFix® is not currently available in the United States.

In the United States, two broad categories of IUDs are commercially available: T-shaped copper IUDs (*e.g.;* ParaGard®) and T-shaped hormone-releasing IUDs (*e.g.;* Mirena®). The goal of our study was to design, fabricate and test a novel inserter and retention device by tethering any commercially available T-shaped intrauterine device to the uterine fundus of an IPP baboon.

2. METHODS

2.1. Prototype Description

Our device consists of an IUD housing tube with a helical needle on one end and a winged knob on the other as shown in Figure 1(a). The winged knob is actuated by the clinician. An introducer tube (Figure 1(b)) shields the helical needle from contacting tissue other than the targeted uterine fundus. The IUD housing tube is fabricated from a clear polycarbonate tube (OD 13 mm × ID 9 mm) 325 mm long. The helical needle is made from a polished 304 stainless steel tube (OD 1.27 mm × ID 0.84 mm) cold formed into a right handed helix (11.2 mm diameter and 5.5 mm pitch), and the needle point is ground to a 3.7 mm bevel. The needle's longitudinal advance depth is restricted to 10 mm.

The needle serves as the tether delivery mechanism, and the clear polycarbonate IUD housing tube secures the IUD (Figure 1(d)) during the insertion procedure. The tether is an intracorporeal barbed absorbable suture (Covidien V-Loc™ 90-day absorbable suture, 3-0 gauge). It is attached to a commercially available T-shaped ParaGard® IUD by threading the IUD's central stem through the loop on the end of the barbed absorbable suture, and advancing the loop to the superior end of the stem as shown in Figure 1(e). The IUD is placed in the inserter and approximately 15mm of the suture is threaded into the helical needle.

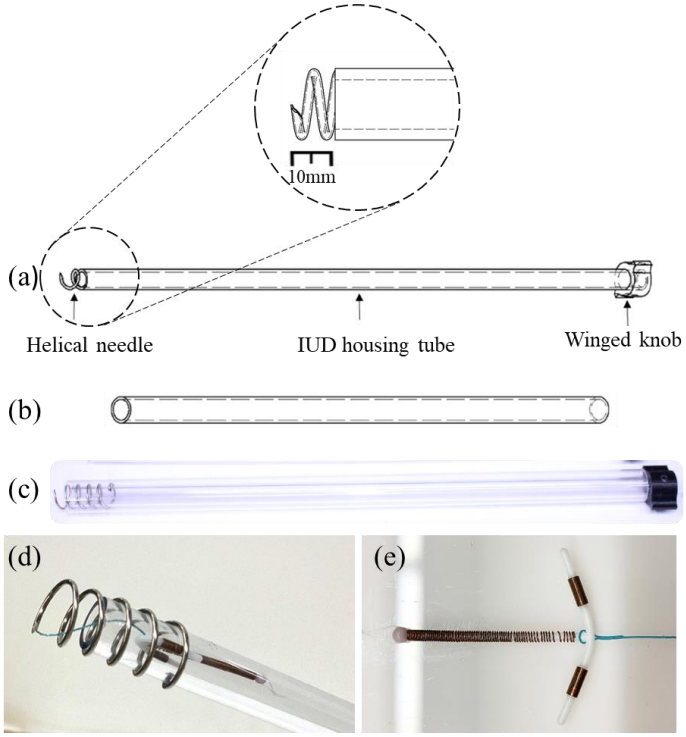

FIGURE 1: NOVEL INSERTER DEVICE. (a) IUD housing tube (b) introducer tube (c) assembled prototype (d) IUD loaded in housing tube (e) Suture loop on the superior end of the IUD's central stem.

2.2. Non-human primate preparation

A single adult postpartum female baboon (Papio Anubis) from a large research colony in the Michael E. Keeling Center for Comparative Medicine and Research was used for this study. This species makes an excellent model for reproductive studies because of its uterine size and the anatomical similarity of its reproductive tract to that of humans [13]. Procedures and instruments (speculums and dilators) used for small women can be used effectively in baboons with no modifications [14]. The baboon was multiparous, and pregnant with a single fetus. Labor was induced at term, 180 days gestational age.

The pregnant baboon, or dame, was placed under general anesthesia. Cervical dilation was assessed, and Misoprostol (two doses of 200 μg, 12 hours apart) was administered intravaginally to induce labor. When labor did not ensue, Oxytocin (20 IU/ml) was delivered intramuscularly every 1-2 hours in the conscious pregnant baboon until the infant was delivered. After the placenta had been delivered (t<3 minutes), Ketamine was administered to sedate the dame for the IUD placement (t<1 hour following placental delivery). The baboon's vagina and perineum were prepared with iodine in preparation for the IUD insertion.

2.3. Experimental procedure

2.3.1. IUD placement experiment

A sterile vaginal speculum was placed in the immediate postpartum baboon and cervix was noted to be dilated. Using a transabdominal approach, ultrasound was used to determine the location and position of the uterus. The IUD introducer tube was placed through the cervix to the uterine fundus using ultrasound guidance. The prepared helical needle inserter was inserted into the introducer tube. Upon contact with the fundus, the insertion tube was rotated clockwise through three half turns (540°) while applying pressure to the winged knob. The insertion tube was then rotated anticlockwise through four half turns, to ensure the needle was completely disengaged from fundal tissue, and the needle inserter was gently retracted from the introducer tube. The introducer tube was removed from the uterus leaving behind only the suture and tethered IUD. Transabdominal ultrasound was used to confirm placement of the IUD at the uterine fundus. A hysteroscope was utilized to directly visualize the intrauterine cavity with the tethered IUD. The dame recovered from anesthesia and was released into her colony.

2.3.2. Ultrasound and hysteroscopy imaging (0, 3 and 6 weeks)

In addition to ultrasound images obtained immediately following device placement, ultrasound images were obtained at follow-up examinations at three and six weeks after the IUD placement procedure to identify uterus and IUD positions.

The primary outcome was the IUD's position at three and six weeks post insertion.

2.3.3. IUD removal

During the 6 weeks when the IUD was inserted, the dame received regular evaluations and was monitored for infection and complications. At the six week time point, the dame was sedated for IUD removal. After the IUD position was visualized using ultrasound imaging, the IUD was removed from the uterine cavity. Ultrasound imaging was used to guide a pair of forceps to grasp the IUD central stem and extract the device from the uterine cavity.

3. RESULTS

Immediately following the insertion procedure, hysteroscopy imaging verified the suture was attached to the myometrium, and visualized IUD position in the uterus.

Three weeks following the insertion procedure, hysteroscopy and ultrasound imaging were used to visualize IUD position in the uterus and verified the tether's attachment to the myometrium (Figure 2).

Six weeks following the IUD placement procedure, a transabdominal ultrasound showed the IUD within the endometrial cavity of the dame's non-pregnant uterus (Figure 3). The central stem is uniformly echogenic and straight within the endometrial cavity, the top of the IUD is in a fundal position, and its inferior end is located furthest away from the fundal wall towards the internal os. A transverse transabdominal ultrasound shows the IUD's arms extended laterally at the uterine fundus (Figure 4).

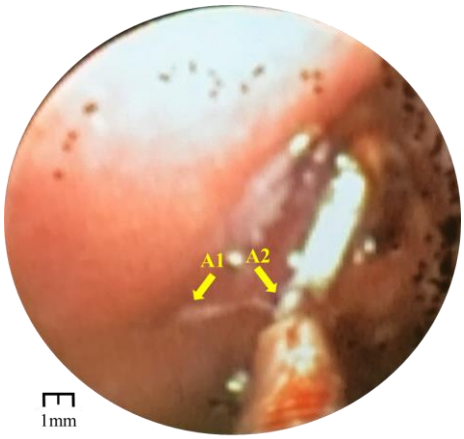

FIGURE 2: 3 WEEK HYSTEROSCOPY IMAGE CONFIRMING TETHER EMBEDDED IN MYOMETRIUM. ARROW A1 INDICATES SUTURE'S POINT OF ATTACHMENT TO UTERINE FUNDUS, ARROW A2 INDICATES SUTURE LOOPED AROUND SUPERIOR END OF IUD CENTRAL STEM

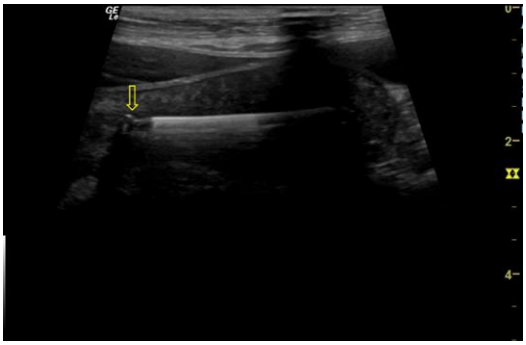

FIGURE 3: SIX WEEK MIDLINE SAGGITAL ULTRASOUND SHOWING UNIFORMLY ECHOGENIC CENTRAL STEM WITHIN ENDOMETRIAL CAVITY. ARROW POINTS TO IUD'S DISTAL END

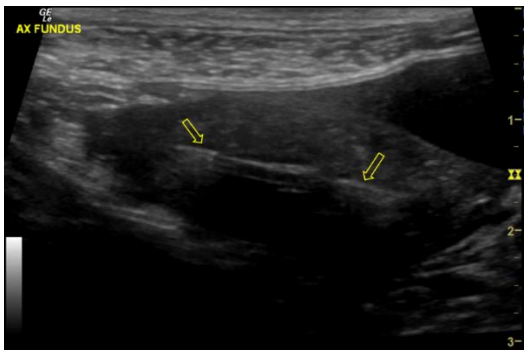

FIGURE 4: TRANSVERSE TRANSABDOMINAL ULTRASOUND SHOWING SUPERIOR END OF THE IUD WITH ARMS EXTENDED LATERALLY AT THE FUNDUS. ARROWS POINT TO ECHOGENIC COPPER BANDS ON THE IUD'S ARMS

4. DISCUSSION

This study demonstrated that it is possible to temporarily and effectively tether a commercially available IUD to an immediately postpartum uterus through a six-week puerperium. At six weeks post insertion, the IUD was located in an ideal position – in close proximity to the uterine fundus with the central stem completely within the endometrial canal [15].

The tether restricted the IUD's displacement from the uterine fundal wall to ~5 mm (Figure 2) in the first 3 weeks following the IUD insertion procedure. Studies have indicated that fundal placement increases IUD retention probability, and minimizes the incidence of displacement and expulsion [16,17]. One study indicated that 25% of copper IUDs inserted in the IPP period were expelled within the first 6 weeks following the insertion procedure [18].

The absorbable suture used in this experiment was shown to degrade in suitable time. At the 3 week mark, the suture was visualized still tethering the IUD to the myometrium, verifying that the suture was secured to the myometrium through initial stages of lochia. At the 6 week mark, the suture was not visualized around the IUD, and the loop through which the central stem was threaded was not present around the stem upon IUD removal, thus suggesting that it had it had been partially absorbed as indicated by the manufacturer [19], or it had been absorbed significantly enough such that it fractured. The Covidien V-Loc™ 90 day absorbable suture was selected because it has been used in surgical obstetric procedures with good results [20,21], and it was important that the suture be suitably absorbed by the 6 week time point so as to not interfere with the IUD's removal. If necessary, a similar suture with a longer or shorter absorption profile could be used in future studies.

The 6-week duration of this experiment was selected to be representative of the typical puerperium duration of 6 weeks.

However, some researchers believe that puerperium lasts longer than 6 weeks [22], and the risk of IUD expulsion lasts well past 6 weeks after the insertion period [18]. Çelen *et al* showed that cumulative IUD expulsion rates rose from 5% at 6 weeks to 12% by the end of the first year following the procedure (n=235) [3]. This could be in part a result of the cyclical growth and thinning of the endometrium which Faúndes *et al* linked to the motion of the vertical stem of the IUD in a non-pregnant uterus [23] during the menstrual cycle, however, a later study indicated that IUDs tend to settle in their final position by the third month after insertion, and this final position may be directly related to the IUD's position at the time of insertion [24].

Ultrasound guided IPP insertions have been shown to correlate with higher retention rates [16,25], specifically because sonography is used to verify that the IUD is in the fundal position. Ultrasound imaging was used to guide the position of our device to the fundus primarily because this was the first time this device was used in a live animal. Our study did not consider the role nor effect of ultrasound guidance in IUD retention, and ultimately, sonography may only be used for measurement, to identify the IUD's position in the endometrial cavity during the course of the experiment.

This study was limited by available budget, therefore the sample size n=1, no control and the duration of the study. It is difficult to design a control for this sort of experiment, as the factors affecting expulsion are not well understood. A longer study would provide more definitive information regarding long term IUD retention as it relates to our temporary tether mechanism.

5. CONCLUSION

In conclusion, our temporary tethering mechanism and method appears to be feasible. A larger and longer study would provide more definitive results regarding the long term safety and efficacy. Though the live animal uterine cavity was smaller than an average human one, the IUD did not migrate nor perforate the uterus, which is a promising result. This method and device would be beneficial to individuals, health practitioners and policy makers, as it could improve access to IUDs in the immediate postpartum period.

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CONFLICTS OF INTEREST

Dr. C. G. Rylander and Dr. Y. Williams-Brown are co-inventors on US patent application number 16/485,957, publication number WO2018/152307. Both inventors have disclosed a financial conflict of interest.

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