INTRODUCTION

Intrauterine device (IUD) is one of the most common contraception methods ***(Aksoy et al., 2016)***. In a survey of female Fellows of the American College of Obstetricians and Gynecologists, the prevalence of personal IUD use was >20-fold higher than among women in the general population ***(Buhling et al., 2014).*** In statistical terms, The IUD is used by approximately 15% of reproductive-aged women in developing countries and 8% in developed countries ***(Searle, 2014).***

This popularity of use has been gained primarily due to high long-term success rates and reversibility. Currently, there is an established evidence about their safety and efficacy. Additionally, they exhibit superior contraceptive potential 20 times over traditionally used oral contraceptive pills that translates to lower rates of unintended pregnancies ***(Karasu et al., 2017)***.

However, the clinical use of IUDs is largely limited by the associated pain during their insertion, which results in little preference of use as contraceptive method from the patient perspective, especially for adolescents and young women. In their observational study, ***Marion et al.*** found that out of 224 nulliparous women, 9% reported no pain, 17% reported severe pain and 72% reported moderate pain during insertion of a levonorgestrel intrauterine system (LNG-IUS) ***(Marion et al., 2011)***.

IUD insertion pain may be felt during various stages of the procedure, including the vaginal examination, placement of the speculum, tenaculum use, traction of the uterus, hysterometry and insertion of the IUD ***(Gemzell-Danielsson et al., 2013)***.

Although being difficult to predict, factors affecting insertion related pain were highlighted explicitly in recent literature. ***Danielsson et al.*** reported that nulliparity, breastfeeding status and time since last pregnancy are the most influential predictors of insertion pain; of these factors, nulliparity is the strongest causal factor ***(Gemzell-Danielsson et al., 2013)***.

Prevention and management strategies of IUD insertion pain include both non-pharmacologic and pharmacologic interventions. Non-pharmacological interventions include pre-insertion counselling, patient reassurance and distraction during the procedure, however, the evidence of efficacy has not established yet ***(Bahamondes et al., 2014)***.

Pharmacologic therapies were largely studied for their efficacy to reduce IUD insertion associated pain. Current pharmacological strategies include: pre-insertion therapy (oral analgesia, cervical ripening/priming and local anesthesia); therapy given during the procedure (local anesthesia administered reactively) and post-procedure therapy (non-steroidal anti-inflammatory drugs and opioid analgesia). Among pharmacologic therapies, amine-anesthetics, like

lidocaine, have been shown to be the most effective for reducing pain during IUD insertion. NSAIDS (Non-steroid anti-inflammatory drugs), which can be used either orally or topically, are common alternatives for reducing the pain felt during IUD insertion, including topical agents like: sprays, gel creams or injectable preparations ***(Akers et al., 2017).***

Pathways of IUD pain can be textualized as pain sensation in the cervix is transmitted to the brain via pelvic splanchnic nerves running through the uterosacral ligaments. All types of lidocaine preparations stabilize the neuronal membrane by inhibiting ionic flow and preventing initiation and conduction of impulses ***(Tavakolian et al., 2015)***.

Lidocaine is an amide compound with aromatic group, 2, 6-xylidine, which is coupled to diethyl glycine via an amide bond. Lidocaine appears to be metabolized chiefly by the liver to 4-hydroxy-2, 6-xylidine and this metabolite is excreted in urine over a 24-hour period and accounts for over 70% endogenous elimination of the administered dose of lidocaine ***(Bauer, 2014)***. Lidocaine was shown to provide analgesia, by blocking both peripheral and central voltage-dependent sodium channels which results in halting the pain impulse initiation and transmission process in the axons ***(Golzari et al., 2014).***

It is generally safe to use topical lidocaine for anesthesia, and adverse reactions are rare. Minor side effects include flushing, redness of the skin, metallic taste and tinnitus ***(Mody***

et al., 2012). Topical lidocaine is contraindicated in patients with a history of hypersensitivity to local anesthetics. Taken together, it is important to reduce the pain experienced during IUD application. Topical lidocaine may be preferred for this purpose. However, There are different results in the literature regarding the efficacy of lidocaine use and degree of patient satisfaction during IUD administration ***(Akers et al., 2017).***

AIM OF THE WORK

The aim of the work is to compare the safety and efficacy of different local lidocaine preparations (spray, cream and injection) for reducing pain associated with IUCD insertion.

Research Question:

In women undergoing IUD insertion, Are lidocaine spray, cream and injection equal in reduction of pain associated with insertion?

Research hypothesis:

In women undergoing IUD insertion, lidocaine preparations (spray, cream and injection) may equally reduce pain associated with insertion.

Chapter 1

INTRAUTERINE CONTRACEPTIVE DEVICE

Introduction:

The intrauterine device (IUCD) is the world's most widely used spacing method of reversible birth control, currently used by nearly 120 million women (about 10-15% of women in reproductive life) ***(Pandey et al., 2015).***

The intrauterine contraceptive device (IUCD) provides long term, reversible contraception equal in efficacy to tubal sterilization ***(Grimes, 2008).***

The IUCD is one of the safest, least expensive and most effective contraceptive devices available. The IUCD is often an excellent choice for women who do not anticipate future pregnancies but wish not to be sterilized. It is a convenient method of contraception; once inserted, it is nearly maintenance-free (except for monthly self-checks to locate the IUCD string) for up to a decade ***(Cetinkaya et al., 2011).***

History of IUCD:

According to popular legend, Arab traders inserted small stones into the uteruses of their camels to prevent pregnancy during long desert treks. The first plastic IUCD, the Margulies Coil or Margulies Spiral, was introduced in 1958. This device was somewhat large, causing discomfort to a large proportion

of women users, and had a hard plastic tail, causing discomfort to their male partners. The modern colloquialism "coil" is based on the coil-shaped design of early IUCD ***(Petta et al., 2005).***

The Lippes Loop, a slightly smaller device with a monofilament tail, was introduced in 1962 and gained in popularity over the Margulies device ***(Lynch and Catherine, 2006).***

Howard Tatum**,** in the USA, conceived the plastic T-shaped IUCD in 1968. Shortly thereafter Dr. Jaime Zipper, in Chile, introduced the idea of adding copper to the devices to improve their contraceptive effectiveness ***(Thiery, 2000*)**.

It was found that copper-containing devices could be made in smaller sizes without compromising effectiveness, resulting in fewer side effects such as pain and bleeding, T-shaped devices had lower rates of expulsion due to their greater similarity to the shape of the uterus ***(Wipf, 2015).***

Tatum developed many different models of the copper IUCD. He created the TCu220 C, which had copper collars as opposed to copper filament, which prevented metal loss and increased the life span of the device. Second-generation of copper-T IUCDs were also introduced in the 1970s. These devices had higher surface areas of copper, and for the first time consistently achieved effectiveness rates of greater than 99 the last model Tatum developed was the TCu380A, the model that is most recommended today ***(Kulier et al., 2008).***

In addition to T-shaped IUCDs, there are also U-shaped IUCDs (such as the Multiload) and 7-shaped Gravigard Copper

7 (with a mini version for nulliparous women introduced in the 1980s). More recently, a frameless IUCD called Gynefix was introduced ***(Wildemeersch et al., 2013).***

The hormonal IUCD was also invented in the 1960s and 1970s. The first model, Progestasert, was conceived of by Dr. Antonio Scommengna and created by Tapani J.V**.** Luukkainen, but the device only lasted for one year of use ***(Thiery, 2000).***

Progestasert was manufactured until 2001. The only commercial hormonal IUCD still currently available, Mirena, was also developed by Dr. Luukkainen and released in 1976 ***(Friend, 2016).***

Now there is the newest IUCD called Skyla, a lower dose IUCD effective for only 3 years, was approved by the FDA in 2013 ***(Beasley and Schutt-Ainé, 2013).***

Metraplant-E is a new intrauterine system recently developed by **Azzam** in 2013, it is a T-shaped frame containing levonorgestrel hormone (60 mg) and Ethylene Vinyl Acetate (120 mg) as well as barium sulfate (20mg) to make it radio-opaque. It is designed with release rate more than 20 ug/day which allow it to be a contraceptive for 5 years , the higher intial release just post application ,up to 28 ug /day has reported by in-vitro studies, may minimize post-insertion bleeding **(Azzam et al.,2014).**

Prevalence:

Globally, the IUCD is the most widely used method of reversible birth control. The most recent data indicates that there are 169 million IUCD users around the world. This

includes both the non-hormonal and hormonal IUCDs. IUCDs are most popular in Asia, where the prevalence is almost 30%. In Africa and Europe the prevalence is around 20%. As of 2009, levels of IUCD use in the United States are estimated to be 5.5% ***(The Guttmacher Institute, 2012).***

Depending on the country, the use of IUCDs worldwide ranges from 2% to 75%. On average, 15% of reproductive-aged women in developing countries and 8% in developed countries use it. Highest rates of utilization are found in China, South east Asia and the Middle East, but as many as 24% of women in select European countries use IUDs ***(D'Arcangues, 2007).***

Data compiled from a US-based study and an international World Health Organization (WHO) study suggested that about 92% of women are still using the Copper T 380A at 1 year after insertion ***(Association of Reproductive Health Professionals [ARHP], 2004).***

Types of IUCD:

Un medicated IUCD (Inert IUCD):

Inert intrauterine contraceptive devices are IUCDs with no bioactive components; they are made of inert materials like stainless steel or plastic materials. Lippes Loop made of plastic impregnated with barium sulfate is still used throughout the world except in United States. Flexible stainless steel rings are widely used in China until 1994 when replaced by copper IUD ***(Bilian, 2007).***

Unmediated IUCDs are approved for use and are popular because they can remain in place for 20 years or more ***(Bilian, 2007).***

They are less effective than copper or hormonal IUDs, with a side effect profile similar to copper IUDs. Their primary mechanism of action is inducing a local foreign body reaction, which makes the uterine environment hostile both to sperm and to implantation of an embryo. They may have higher rates of preventing pregnancy after fertilization, instead of before fertilization, compared to copper or hormonal IUDs ***(Ortiz, 2007).***

The pregnancy rates for both the Lippes Loop and Stainless steel ring are greater than 2 pregnancies per 100 women.The higher failure rate of the Stainless steel ring lead the Chinese State Family Planning Commission to encourage the use of Copper or LNg-releasing IUCDs instead ***(Bilian, 2007).***

Medicated IUCDs:

Chemically active devices have continuous elution of copper or progesterone agent.

Figure (1): Hormonal and Copper IUCD.

Non hormonal copper IUCD:

There are a number of models of the copper IUCD available around the world. Most copper devices consist of a plastic core that is wrapped in a copper wire ***(Kulier et al., 2008).***

Copper IUDs are becoming increasingly popular because they are more resistant to corrosion. Copper IUDs are also available in a wider range of sizes and shapes than hormonal IUDs.

The first copper IUDs were wound with 200 to 250 mm2 surface area of wire, and two of these are still available; The TCu-200 and multiload 250n. The more modern copper IUDs contain more copper, and part of the copper is in the form of solid tubular sleeves rather than wire, increasing efficacy and extending life span ***(Bilgehan et al., 2015).***

The Nova T is similar to the TCU-200, containing 200 mm2 of copper, however, the Nova T has a silver core to the copper wire, flexible arms, and large, flexible loop at the bottom to avoid injury to cervical tissue ***(Kortesuo et al., 2013).***

The TCU-380 A (the para Gard) is a T-shaped device with a polyethylene frame holding 380 mm2 of exposed surface area of copper that provides contraception for at least 10 years. This IUCD is 100% hormone-free and doesn't alter the menstrual period. It's made of plastic and a small amount of natural, safe copper ***(Kulier et al., 2008).*** The Paragard T Cu

380A measures 32 mm (1.26") horizontally (top of the T), and 36 mm (1.42") vertically (leg of the T). The IUD frame contains barium sulfate, making it radiopaque.

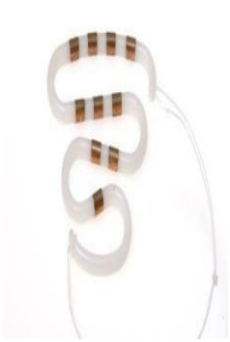
Copper IUCD containing noble metals are becoming increasingly popular because they are more resistant to corrosion. In the "Gold T IUCD", which is made in Spain and Malaysia, there is a gold core, which further prevents the copper from fragmenting or corroding. Goldring Medusa is a differently shaped German version of the Gold T ***(Winner et al., 2012).***

Another form of Au Cu IUCD is called Goldlily. Goldlily consists of a layer of copper wires wrapped around an original layer of gold wires, and it provides electrochemical protection in addition to ionic protection ***(World Health Organization, 2010).***

Silver IUCD is similar to Goldlily, and Goldring Medusa is available in an Ag Cu version as well. Nova-T 380 contains a strengthening silver core, but does not incorporate silver ions themselves to provide electrochemical protection ***(NetDoctor, 2006)***.

Other shapes of IUCD include the so-called U-shaped lUCDs, such as the Load and Multiload, and the frameless IUCD ***(Nova T3S0 Patient Information Leaflet, 2007).***The mulitload-375 has 375 mm2 of copper wire wound around its stem. The flexible arms were designed to minimize expulsions ***(Belden et al., 2012).***

Frameless IUCDs contain either copper or levonorgestrel that has been attached to a non-resorbable filament. The GyneFix 330 is made up of copper cylinders threaded onto a polypropylene suture instead of the plastic frame common to other IUCDs. The FibroPlant is a frameless levonorgestrel-releasing IUCD consisting of a non-resorbable thread attached to a fibrous delivery system that releases 14 to 20 mcg of levonorgestrel per day. Advantages of these systems include small size, high efficacy, and high tolerability. They are as effective as conventional IUCDs and may be more adaptable to variations in the shape of uterine cavity ***(Wildemeersch, 2007).***



A)Lippes loop

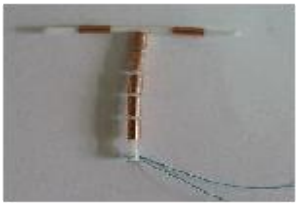
b)Multiload IU

c)Gynefix IUD

d)Nova T IUD

e) TCu200

f) TCu 380



g) TCu 220

Figure (2): Different Types of IUCDs

Duration of usage:

The TCu380A is approved to remain in place for 10 years. However, this may vary elsewhere. The use of the TCu380A beyond 10 years is supported by several studies ***(Bahamondes et al., 2005).***

Efficacy of copper IUCD:

With perfect use, the probability of pregnancy in the first year is 0.6 percent; with typical use, the first year pregnancy rate is 0.5 to 0.8 percent ***(Heinemann et al., 2016).***

Reasons to choose copper IUCD (advantages of copper IUCDs over LNg IUCDs):

- Avoidance of exogenous hormones: the copper IUCD contains no hormones and may be used by women who want or need to avoid exogenous hormones (i.e., women within five years of breast cancer treatment) or women who do not want hormone-induced side effects (e.g., headache, and mood change).
- Fertility returns quickly after removal.
- Can be used with breast feeding.
- Continuation of endogenous menstrual cycle: the Copper IUCD does not cause anovulation or amenorrhea. Copper IUCD users continue to have cyclic menstrual bleeding and have less unscheduled bleeding or spotting than LNg IUCD users.

- Desire for long-term contraception: The TCu380A is approved for more years of use than LNg IUCDs (10 years for the TCu380A versus three to five years for LNg IUCDs).
- Need for emergency contraception: the TCu380A can be inserted for emergency contraception up to five days after unprotected sex, and then left in place to provide ongoing contraception. It is the most effective form of emergency contraception available.

(Heinemann et al., 2016)

Side effects of Copper IUCD:

Women considering the copper IUCD are counseled that menses may be heavier, longer, or more uncomfortable, particularly in the first several cycles after insertion. These symptoms are improved rapidly. Non-steroidal anti-inflammatory drugs (NSAIDS) appear to decrease menstrual blood loss, bleeding duration and associated pain ***(Diedrich et al., 2015).***