Oral Tiemonium Methylsulfate versus Placebo for Pain Relief before Outpatient Hysteroscopy: A Randomized Controlled Trial

Thesis

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Mohamed Ekrema Helmy Koota

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List of Abbreviations

Abb.	Full term
5-HT	*5-hydroxytryptamine*
ACOG	*American College of Obstetricians and Gynecologist*
BMI	*Body Mass Index*
CO_2	*Carbon dioxides*
COX	*Cyclooxygenase*
CRF	*Case Record Form*
DBP	*Diastolic Blood Pressure*
ECDU	*Early Cancer Detection Unit*
GABA	*Gamma-Aminobutyric acid*
HR	*Heart Rate*
IASP	*International Association for the study of Pain*
IM	*Intramuscularly*
IUD	*Intrauterine device*
IV	*Intravenous*
KTP	*Potassium – Titanyl – Phosphate*
Nd:YAG	*Neodymium:yltrium-Aluminium-Garnet laser*
NMDA	*N-methyl D-Aspartate*
NRM	*Nucleus Raphe Magnus*
NSAIDs	*Nonsteroidal anti-inflammatory drugs*
OD	*Outer Diameter*
PAG	*Peri-Aqueductal Grey matter*
PG2	*Prostaglandin 2*
PO	*Per Oris*

List of Abbreviations (Cont...)

Abb.	Full term
RCTS	*Randomized controlled trials*
RR	*Respiratory Rate*
SBP	*Systolic Blood Pressure*
Sc	*Subcutaneously*
SD	*Standard Deviation*
SSRIs	*Selective serotonin re-uptake inhibitors*
TENS	*Transcutaneous Electrical Neural Stimulation*
VAS	*Visual analogue scale*
VMM	*Ventromedian Medulla*
WDR cell	*Wide dynamic range cells*

Chapter 1

HYSTEROSCOPY

Historical background:

B*ozzini (1773-1809),* a German, was the first to invent endoscope. His light conductor was a hollow tube divided by a vertical septum fitted with a concave mirror that, by transmitting the light of a candle, permitted the visualization and exploration of externally accessible body cavities such as the mouth, nose, ears, vagina, cervix and uterus, urethra and urinary bladder, and rectum ***(Van der Pas et al., 1983).***

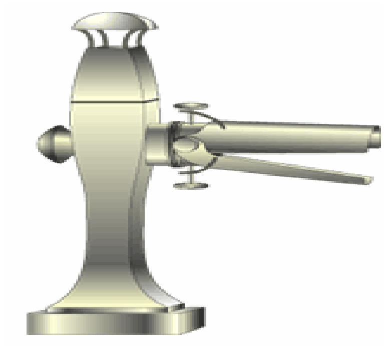

Fig. (1): Bozzini's endoscope displayed at the American College of Surgeons headquarters in Chicago ***(Valle, 2007).***

The French ***Désormeaux*** presented the first truly workable cystoscope in ***1853***. It allowed a direct view through a central perforation, and light from an alcohol and turpentine lamp reflected by a concave mirror inserted in a viewing tube ***(Désormeaux, 1855).***

Sixteen years later, particularly in ***1869, Pantaleoni***, using Desormeaux's cystoscope, performed a hysteroscopic examination in a postmenopausal woman with abnormal uterine bleeding and reported that he found a polypoid growth in the uterus and cauterized it under hysteroscopic view with silver nitrate.

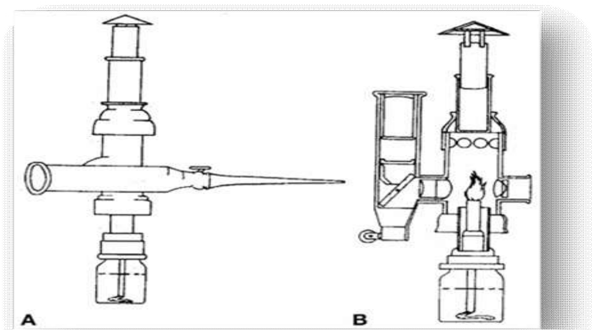

Fig. (2): Diagram of Desormeaux's endoscope. (A) Endoscope. (B) Sagittal view showing flame and reflecting lens ***(Valle, 2007)***.

In ***1879, Nitze*** introduced his cystoscope, in which distal illumination was provided by a platinum loop cooled with fluid circulating around the endoscope. The fact that; the thin-walled urinary bladder could be distended by gravity pressure and, unlike the uterus, didn't bleed on contact, helped the cystoscopy soon to be made practical following the introduction of Nitze's cystoscope. However, hysteroscopy remained unpopular and troublesome**.**

So, although other physicians followed suit after Pantaleoni's first known hysteroscopic diagnosis and treatment, they were faced by some obstacles including; inadequate light transmission, bleeding inside the uterus, and the inability to distend the organ properly. These factors slowed the development and applications of hysteroscopy. ***David, in 1907,*** developed the first contact hysteroscope.

It was clear that a practical method of viewing the uterine cavity should provide a panoramic view similar to that of cystoscopy, thus, it required intrauterine distension. ***Heineberg in 1914 and Seymour in 1926*** introduced an endoscope that had an internal channel for illumination and contained a system of irrigation with low viscosity fluids to wash any blood and permit uterine distension. This method was the beginning of continuous-flow hysteroscopy and the basis for all such methods introduced later on.

During the next few years, most physicians preferred working with low-viscosity fluids, although ***Rubin*** reported on his experience and excellent results when he used carbon dioxide to distend the uterine cavity for hysteroscopy. Nonetheless, the use of this gas remained rare ***(Rubin, 1925).***

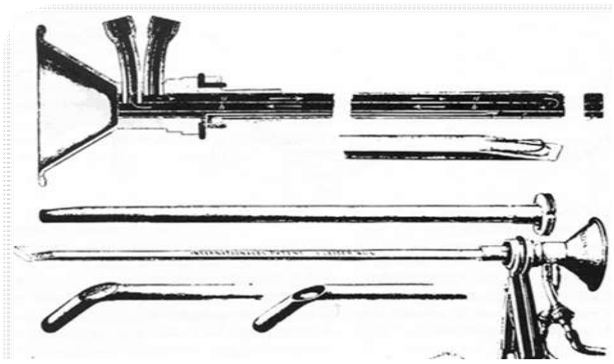

Fig. (3): Nitze's early endoscope with a platinum loop for illumination (1879) ***(Valle, 2007).***

The greatest improvements in distension media took place in the early 1970s when ***Edstrom and Fernstrom (1970)*** utilized successfully a high molecular weight dextran, meanwhile, ***Quinones-Guerrero et al. (1970)*** initiated the use of dextrose 5% in water delivered under pressure as a distension medium, till ***Lindemann (1972)*** re-introduced Rubin's technique of carbon dioxide gas insufflation.

In 1979, ***Hamou*** revolutionized the field of hysteroscopy and further popularized the use of hysteroscopy in 1980s and 90s ***(Hamou, 1981).***

No significant technologic improvements were reported in the field of hysteroscopes throughout the 1980s. Moreover, electronic devices, such as electronic pumps or endocameras, were not available at a reasonable price. At the beginnings of 1990s, new scopes began to be introduced allowing the physician to adopt an operative scope equipped with mechanical instruments even for a diagnostic procedure ***(Bettocchi et al., 2004).***

Hysteroscopy is an endoscopic procedure that has become an important tool to evaluate intrauterine pathology, it offers a direct visualization of the entire uterine cavity including the openings to the Fallopian tubes, as well as direct examination of the cervix, cervical canal and vagina and also provides the possibility of performing biopsy of suspected lesions that can be missed by dilatation and curettage (D&C) ***(Bradley, 2010).***

In most cases, the intrauterine pathologies can be diagnosed and treated at the same setting as office hysteroscopy; for example: endometrial polyps can be diagnosed and removed; similarly, intrauterine adhesions can be liberated in the outpatient setting without the need for an operating theatre ***(Sussan et al., 2015).***

Types of hysteroscopy:

- ***The flexible hysteroscope:***

Flexible (fiberoptic) hysteroscopes range in diameter from 2.7 mm to 5 mm and have a bendable tip that can be deflected in two directions ranging from 120 degrees to 160 degrees (Figure 4), it's also contain an operating channel for tubal catheterization or endometrial biopsy ***(Breitkopf et al., 2012).***

The flexible hysteroscope is most commonly used for office hysteroscopy, it's most appropriate use is to accommodate the irregularly shaped uterus and to navigate around intrauterine lesions ***(Groenman et al., 2015).***

They generally do not require cervical dilation, and have a longer working length than rigid hysteroscopies ***(Cheong and Ledger, 2007).*** The smaller outer diameter (OD) compared to a rigid hysteroscope is advantageous in patients with nulliparity or prior cervical conization, and the longer working length is helpful in morbidly obese patients ***(Greenfield et al., 2008).***

Fig. (4): Karl Storz flexible hysteroscope ***(Bradley and Tommaso, 2009).***

- **The rigid hysteroscope:**

Rigid hysteroscopies are wide range of diameters allows for in-office and complex operating-room procedures. Narrow options (3-5 mm in diameter), the 4-mm telescope (lens) offers the sharpest and clearest view ***(Bradley and Tommaso, 2009)***.

It accommodates surgical instruments but is small enough to require minimal cervical dilation (Figure 5) ***(Petrozza and Attaman, 2010).***

Operative hysteroscopy typically range from 8 mm to 10 mm in diameter and contain a working element, which require increased cervical dilation for insertion ***(Bradley, 2010).***

Therefore, they are most frequently used in the operating room with intravenous (IV) sedation or general anesthesia ***(Petrozza and Attaman, 2010).***

An outer sheath fits over the telescope to introduce and remove distending media from the intrauterine cavity and to provide ports to accommodate large and varied surgical instruments ***(Breitkopf et al., 2012).***

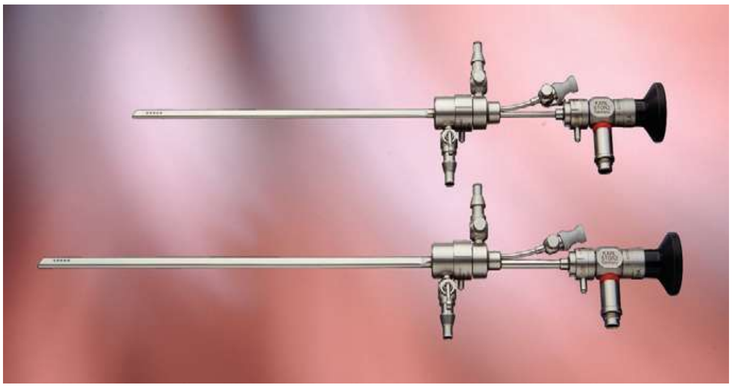

Fig. (5): Rigid hysteroscopes ***(Bradley and Tommaso, 2009)***

Parts of Hysteroscopy

The hysteroscope consists of 3 parts: the eye piece, the barrel, and the objective lens. The focal length and angle of the distal tip of the instrument are important for visualization ***(Critchley et al., 2004).***

Angle options include: 0°, 12°, 15°, 30° and 70°, which 0° hysteroscope provides a panoramic view, whereas angled one might improve the view of the ostia in an abnormally shaped cavity ***(Petrozza and Attaman, 2010).***