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Modern endoscopic-based exploration of the female reproductive tract: a model for developing countries?

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Introduction

Infertility has been notorious for its time-consuming and prolonged explorations and the resultant delay in diagnosis. This delayed diagnosis adds to the burden of the patient and, in spite of the higher pregnancy rate and lower cost reported with traditional treatment algorithm as first-line therapy compared with liberal referral to assisted reproduction technologies (ART) (Karande *et al*., 1999), has stimulated physicians and specialized centres to promote the latest approach. This strategy has the additional problem, especially for developing countries, that ART carry a higher risk of neonatal and maternal morbidity than natural conception, even in the absence of multiple pregnancy (Helmerhorst *et al*., 2004; Ombelet *et al*., 2005, 2006).

Recent observations demonstrate that exploration of the female reproductive tract is not only useful for diagnosis and treatment but also necessary for enhancing the *in vitro* fertilization—embryo transfer (IVF-ET) results. Indeed, a Cochrane review including three RCT shows that laparoscopic salpingectomy prior to IVF-ET in patients with hydrosalpinges improves pregnancy, ongoing pregnancy and live birth rates (Johnson *et al*., 2002). Furthermore, the incremental cost of the surgical intervention to achieve this higher live birth rate was reported to be beneficial (Strandell *et al*., 2005).

Everybody agree on the value of an accurate exploration of the female reproductive tract for the management of infertility but opinions greatly differ as how and to which extent these investigations should be performed. In current practice hysterosalpingography (HSG) is still used as a first-line investigation, although it is not a pain-free (Tur-Kaspa *et al*., 1998) and risk-free procedure and even when its sensitivity, specificity and prognostic values for the management of the infertility are debatable (Glatstein *et al*., 1997; Swart *et al*., 1995; Mol *et al*., 1997, 1999). This option is largely based on the absence of alternatives since endoscopic procedures (e.g. conventional laparoscopy and hysteroscopy) demanding high skills and sophisticated equipments do not fulfil the criteria of being minimally invasive, affordable and accessible.

Although conventional laparoscopy is considered the gold standard for the exploration of the female reproductive tract, it is for several reasons not suitable as a first-line investigational technique. Laparoscopy is an expensive procedure requiring hospitalization, operating room and general anaesthesia, as in open abdominal surgery. The procedure is invasive and not without morbidity and mortality. Indeed, even in experienced hands the blind transabdominal access can cause major blood vessel and bowel injury (Jansen *et al*., 1997; Brosens *et al*., 2003), whereas the distension medium (i.e. CO2 pneumoperitoneum) causes discomfort and additional hazards (Molinas and Koninckx, 2000; Molinas *et al*., 2001; Nguyen *et al*., 2002; Kissler *et al*., 2004). Furthermore, the see-and-treat possibility of laparoscopy requires the presence of a high skilled reproductive surgeon at the diagnostic screening procedure, which is not always feasible.

The exploration of the female reproductive tract should be as easy as HSG and as accurate as standard laparoscopy. No conclusive answer has been given until now, but the transvaginal ultrasound and endoscopic procedures offer probably the most efficient and accurate solution to the problem. The challenge is for both developed as developing countries identical: to find a low cost and easily accessible diagnostic procedure with operative possibilities for offering the fastest and minimal invasive lane to pregnancy.

In this article we outline a challenging concept for the management of infertility in both developed and developing countries: a model based on ambulatory endoscopic techniques (i.e. modern mini-hysteroscopy and transvaginal laparoscopy) for the exploration of the female reproductive tract, describing their diagnostic and operative possibilities and limitations.

Ambulatory endoscopic exploration of the female reproductive tract

In order to propose the systematic use of transvaginal endoscopic procedures, such as mini-hysteroscopy and transvaginal hydro-laparoscopy (TVL), and to avoid the still well-established delay in indication, it is mandatory to perform the technique in an easily accessible ambulatory environment, ideally at the same time as the transvaginal sonography (TVS). The most important challenge for this approach is to

be able to perform the procedure with an acceptable patient compliance, high accuracy and low complication rate. The scientific evidence gathered over the last years and the major technical improvements in the manufacturing of high-quality small-bored scopes have indicated how diagnostic hysteroscopy should be performed in the office. Although TVL requires advance endoscopic skills, the required basic skills and instrumentation are similar to those required for hysteroscopy.

Endoscopic materials and instruments

Distension media

Low viscosity fluids with electrolytes (e.g. saline, Ringer lactate) are used for uterine or abdominal distension during hysteroscopy and TVL, respectively. In contrast with CO2, fluids are easier to use and offers better patient compliance and excellent visualization capacity due to the rinsing and the hydroflotation (i.e. lesions floating in the watery low pressure environment) effects. To control pressure and flow a simple gravity fall system or a pressure cuff can be used.

Endoscopic hardware

All-in-one equipments are available for ambulatory procedures. They have the advantages of being easily transportable with acceptable cost–efficiency ratio. The TELE PACK (Karl Storz) is a comprehensive, multifunctional and compact documentation terminal that can be used as a compact system in the doctor's office or as a secondary system in the operating room consisting of an input unit (inbuilt, high-quality membrane keyboard and text generator for entering patient data), documentation (flexible, all-purpose PCMCIA memory card for recording still images; easy transfer of data to AIDA and PC), camera control unit, illumination (HiLux high-performance light source) and image display (foldaway LCD colour monitor).

Endoscopes and diagnostic shafts

The optics available are the 2.9 and the 2.0 mm (for mini-hysteroscopy) 30° forward-oblique rigid telescopes. For diagnostic purposes the former is used with a single-flow diagnostic sheath of 3.7 mm (hysteroscopy and TVL), whereas the latter is used with a single-flow diagnostic sheath of 2.8 mm (hysteroscopy). Both diagnostic sheaths have a round shape.

Operative shafts for hysteroscopy

For operative purposes the mentioned optics can be assembled in a single- or double-flow operative sheath of 4.2 or 5.0 mm, respectively. Theses operative sheaths have an oval shape to reduce the instrument diameter as much as possible and a working channel for 5 Fr instruments.

System for diagnostic TVL

The system includes a puncture needle (diameter 1.5 mm, length 30 cm) with automatic spring mechanism, the dilation sheath (diameter 3.8 mm, length 30 cm) and the trocar sheath (diameter 4.4 mm, length 20 cm). The system is assembled with the needle inside the dilation and both inside the trocar. The length of the needle tip can be preset at 10–25 mm.

Operative shaft system for TVL

For operative procedures an operative sheath (diameter 6.6 mm) with an atraumatic tip and a working channel for 5 Fr instruments is used. A guide mandrin (diameter 2.9 mm) is used to replace the diagnostic sheath for the operative one.

Accessory 5 Fr instruments for both operative hysteroscopy and TVL

Mechanical (e.g. crocodile grasping forceps, spoon and punch biopsy forceps, sharp and blunt scissors) and electrical (e.g. bipolar needle, bipolar coagulation probe) instruments are available.

Disinfection of instruments

Although the vagina is a non-sterile environment the implementation of ambulatory hysteroscopy depends on the inter-procedure instrument disinfection capacity. The disinfection procedure should be rapid and suitable for performing in the same room where the endoscopic procedure is performed. The disinfection product should be non-toxic (i.e. aldehyde-free), biodegradable, effective against all kinds of micro-organisms, inclusive resistant spores, cheap, easy to use, instrument friendly. Tristel fusion (Tristel Solutions Limited) is a disinfecting solution for medical devices including instruments such as endoscopes and it is proven to be effective against bacteria, fungi, viruses and even the most resistant spores in a very short contact time (5 min).

The ambulatory approach reduces cost significantly

Infertility exploration is a demanding condition both personally and financially. Current estimates are that 10.7% of couples in the US between 18 and 45 years seek care for infertility and that the total costs for evaluating and caring for the infertile couple amounts to 3 billion US$ (Wilcox and Mosher, 1993). Laparoscopy has a high yield but can amount up to 70% of the total infertility evaluation cost (Bates and Bates, 1996). Undoubtedly, the impact and actual monetary expense of the infertility evaluation could be reduced by prompt and efficient office evaluation.

The above described instrumentation set up provides a full operational endoscopic unit for not more than the price of a cheap ultrasound machine. The running costs are moreover very low when only reusable instrumentation is used and the fast low cost disinfection procedure offers the possibility to reduce the total amount of instruments necessary for a working day.

The primary use of TVL for infertility management would eliminate hospital costs. The benefit depends on the rate of conversion to standard laparoscopy. The increasing use of office operative TVL (e.g. ovarian drilling) (Fernandez *et al*., 2001; Moore and Cohen, 2001; Gordts *et al*., 2002, 2004) is likely to boost the cost–benefit of TVL over laparoscopy.

Hysteroscopy

Technique

The examination starts with TVS to evaluate the uterus and the adnexal region. Then, vaginal disinfection with a

non-irritating watery solution is performed without placing a speculum. The tip of the mini-hysteroscope is positioned in the vaginal introit and the vagina is distended with the same medium used for the uterine cavity. The scope is driven to the posterior fornix to visualize the portio and slowly backwards to identify the external cervical os. When this is visible, the scope is introduced into the cervical canal and after achieving its distension the scope is carefully moved forward to the internal cervical os and then to the uterine cavity. The anatomical landmarks (i.e. tubal ostia) and the uterine fundus and walls (i.e. laterals, anterior and posterior) are systematically explored by rotating the 30° fore-oblique scope. The technique requires a good knowledge of the physics and instrumentation as well as dexterity from the operator (i.e. the correlation between what is seen in the screen and the actual position of the 30° scope) to avoid unnecessary movements and to reduce patient discomfort (Campo *et al*., 1999a, b). Immediately after the hysteroscopy, a second TVS is performed taking advantage of the intracavity fluid for a contrast image of the uterus.

Feasibility of diagnostic hysteroscopy

To evaluate the factors influencing the success rate of office diagnostic hysteroscopy, we have conducted a RCT including 480 patients (Campo *et al*., 2005). The effects of instrument diameter (conventional hysteroscopy: 4.0 mm optic with 5.0 mm sheath or mini-hysteroscopy: 2.7 mm optic with 3.5 mm sheath), patient parity (with or without vaginal deliveries) and surgeon's experience (with or without experience in office hysteroscopy) were evaluated. The following variables were assessed: pain [10-cm visual analogue scale, 0 (no)–10 (intolerable)], quality of visualization of the uterine cavity (0, no; 1, insufficient; 2, sufficient; 3, excellent) and complication rate. The procedure was considered successful only when pain was <4, visualization was sufficient or excellent and when no complications occurred. In comparison with conventional hysteroscopy, mini-hysteroscopy was associated with less pain and better visualization. Due to the overall low complication rates, no differences could be detected between both groups. The success rate of mini-hysteroscopy (87%) was significantly higher than of conventional hysteroscopy (44%). In a multifactorial analysis, pain, visualization and success rate were highly influenced by instrument diameter and patient parity and only slightly influenced by surgeon's experience. A better performance was observed with the use of mini-hysteroscopy, in patients with vaginal deliveries and in procedures performed by experienced surgeons. The effects of patient parity and surgeon's experience were even more significant when conventional hysteroscopy was performed. This was not surprising since in those patients and in those surgeons an easier access to the uterine cavity and less traumatic manoeuvres, respectively, can be expected. Interestingly, both patient parity and surgeon's experience were no longer important when mini-hysteroscopy was performed, indicating that a small diameter endoscope can counteract the difficulties determined by the anatomy and by the operator (Campo *et al*., 2005).

Hysteroscopic findings

The findings are recorded in a standardized pre-design form. A complete visualization of cervical canal, uterine cavity and tubal ostia and absence of any anatomical alterations is required to categorize the examination as normal. It is considered abnormal when major or minor lesions, regardless their clinical significance, are detected (Molinas and Campo, 2006). If the visualization is insufficient for any reason, it is stated that the examination failed to achieve a diagnosis.

Major lesions

Major lesions are arbitrarily defined as those that structurally change the normal hysteroscopic anatomy (e.g. cervical stenosis, endocervical polyps, submucous myoma, endometrial polyps, congenital malformations, adhesions, necrotic tissue, tubal os stenosis, foreign bodies) (Molinas and Campo, 2006).

Minor lesions

Minor lesions or subtle lesions are those changes of the appearance without deformation of the normal anatomy, where the clinical significance is not always proven but where the hysteroscopic picture is different from the normal situation (e.g. diffuse polyposis, hypervascularization, strawberry pattern, moderate/marked localized/generalized mucosal elevation, endometrial cysts or greets) (Molinas and Campo, 2006).

In the infertile patient these lesions can be the (co)factor of the infertility or at least impairs the results of ART treatments. In a recently published RCT including 480 infertility and AUB patients we observed normal findings in 55% of the cases and abnormal findings in 41% of the cases, whereas no diagnosis could be obtained in 4% of the cases (Campo *et al*., 2005). Interestingly, normal and abnormal findings were not equally distributed in patients with infertility or AUB. Indeed, in infertility patients the findings were normal in 67% of the cases and abnormal in 29% of the cases, whereas no diagnosis could be obtained in 4% of the cases. In AUB patients, however, the findings were normal in only 46% of the cases and abnormal in 51% of the cases, whereas no diagnosis could be obtained in 3% of the cases. Furthermore, the specific findings were significantly different in both groups of patients (Molinas and Campo, 2006).

Operative hysteroscopy

Pathologies causing or contributing to the infertility, or at least impairing the ART results, detected during diagnostic hysteroscopy can be, depending on the nature and severity of the abnormality, either treated in the same set up or scheduled for treatment in the conventional operating room.

Cervical stenosis, small endocervial or endometrial polyps, lost foreign bodies (e.g. IUD), some uterine adhesions and congenital anomalies (i.e. uterine septum and T-shaped uterus) can be treated in an ambulatory setting with or without some sort of analgesia or sedation, according to the severity of the pathology, the characteristics of the patient, the experience of the surgeon and the available facilities. Since treatment is done with the same distension medium only bipolar instruments can be used for thermal energy.

Transvaginal hydro-laparoscopy

Indications for diagnostic TVL

TVL, one of the earliest examples of Natural Orifice Transluminal Endoscopic Surgery (NOTES) (Gordts *et al*., 1998), is indicated for the exploration of the reproductive tract in patients with primary or secondary infertility without any obvious pathology at an early stage of the infertility exploration, making the use of HSG unnecessary. Contraindications for the procedure are intact hymen, narrow vagina, acute infections, obliterated cul de sac, fixed retroverted uterus, extreme obesity, haemoperitoneum and tumours prolapsed in the pouch of Douglas.

Technique for diagnostic TVL

The procedure is performed in the same ambulatory setting with the patient in dorsal lithotomy position. A vaginal examination and TVS are performed to assess the size and position of the uterus and to exclude any contraindications of the procedure. The vagina is disinfected and a hysteroscopy is performed, as described above (Campo *et al*., 1999a, b). Then, a Collin speculum is placed in the vagina and local anaesthesia is applied in the centre of the posterior fornix and in the posterior lip of the cervix, which is grasped and pushed forwards. The specially designed needle-dilating-trocar system is placed in the midline at 10–15 mm below the insertion of the vaginal wall on the cervix. According to the characteristics of the patient, the needle is pre-set (usually at 15 mm) and inserted using the spring load system. Then, dilator and trocar are pushed forward to enter into the abdominal cavity using the needle as a guide. The right intra-abdominal position of the trocar is confirmed visually and then the fluid distension medium is slowly introduced (Gordts *et al*., 1998).

In contrast to standard *trans*-umbilical CO2 laparoscopy, panoramic view cannot be obtained, making necessary a strict standardization of the procedure, as described previously (Gordts *et al*., 1998; Campo *et al*., 1999a, b). After recognition of the posterior uterine wall (primary anatomical landmark), the optic is rotated and directed towards either the left or the right side to individualize the utero-ovarian ligament and the istmical portion of the tube (secondary anatomical landmark). Then, the tube is inspected going downwards in direction of the fimbria. The entire ovarian surface and the pelvic side wall, including the ovarian fossa, are also examined. A salpingoscopy is also performed when feasible. The same procedure is performed to explore the contra-lateral side. Finally, the utero-sacro ligaments are inspected and the tubal patency is checked by the intra-uterine instillation of diluted methylene blue.

The fluid used during the procedure (normally 200–400 ml) should be removed at the end of the examination through the trocar. The puncture site in the posterior fornix is not sutured unless there is active bleeding. Patients are informed that some vaginal leakage or bleeding may occur and are advised to do not use vaginal tampons and to abstain from intercourse for some days.

Feasibility of diagnostic TVL

The initial experience with diagnostic ambulatory TVL under local anaesthesia was evaluated to determine the feasibility of the procedure (Gordts *et al*., 2000). Out of the first 157 patients with primary or secondary infertility undergoing the procedure, access to the abdominal cavity was achieved in 94.5% of the cases and not possible in 4.6% of the cases. In 0.9% of the cases the procedure was aborted due to complications. The feasibility has then been confirmed by several authors (Watrelot *et al*., 1999; Bajzak *et al*., 2000; Darai *et al*., 2000; Dechaud *et al*., 2001; Moore and Cohen, 2001; Verhoeven *et al.*, 2004).

Patient compliance for diagnostic TVL

During the initial experience with TVL, 60 consecutive patients were asked to rank the pain experienced during the examination at the end of the procedure on a 10 cm visual analogue pain scale. The pain score (mean $\pm$ SD) was 2.7 ± 1.5, in 8% of the cases the score being >5. Ninety-six per cent of the patients agreed to repeat the procedure under the same circumstances if this would be required (Gordts *et al*., 2000).

Other authors reported similar figures (Moore *et al*., 2003) and concluded that TVL together with hysteroscopy under local anaesthesia was better tolerated than HSG (Cicinelli *et al*., 2001).

Accuracy of diagnostic TVL

The accuracy of the technique for the diagnosis of tubo-ovarian pathology in infertility has been widely reported (Watrelot *et al*., 1999; Bajzak *et al*., 2000; Darai *et al*., 2000; Dechaud *et al*., 2001; Moore and Cohen, 2001; Shibahara *et al*., 2001).

In a prospective study, 10 patients were explored by two different endoscopists with both TVL and standard laparoscopy. The inter-observer agreement for ovarian adhesions was 75% for standard laparoscopy and 90% for TVL (Campo *et al*., 1999a, b).

In patients with mild endometriosis more ovarian adhesions were detected with TVL than with standard laparoscopy (Brosens *et al*., 2001). These non-connecting filmy adhesions, which clinical significance still requires further investigation, could be detected with TVL due to the hydroflotation, but not with standard laparoscopy because the pneumoperitoneum flattered and masked them against the surface of the ovary or the abdominal wall.

For the diagnosis of tubal patency, 95% of agreement between TVL and HSG was reported (Cicinelli *et al*., 2001). In the same study a bilateral spilling of the methilen blue was seen at TVL in a case of bilateral proximal obstruction previously diagnosed at HSG. Other authors failed to find differences for tubal patency between HSG and TVL but found that TVL was superior for the diagnosis of peritubal adhesions (Shibahara *et al*., 2001).

Safety of diagnostic TVL

The transvaginal access for pelvic endoscopy was initially used in culdoscopy, but due to the higher incidence of bowel injury and risk of sepsis it was abandoned in favour of standard laparoscopy (Copenhaver, 1970). Although the access of TVL is similar to culdoscopy, the technique differs because of the use of small instruments, the patient position, the non-irritant saline distension medium and the absence of exteriorization for surgical procedures. Nevertheless, concern has been

expressed for the risk of bowel injury and sepsis. The TVL needle-dilator-trocar system was specially designed to minimize the injury by the blind insertion of the instruments and the consequences of possible injuries, such as infection, rectum perforation, bleeding and uterus puncture.

A multinational survey evaluating the risk and outcome of bowel injury during TVL registered 24 bowel injuries in 3667 procedures (0.65%). After the initial experience, the prevalence of this complication decreased to 0.25%. There was no delayed diagnosis and all injuries were managed expectantly without complications (Gordts *et al*., 2001).

To evaluate the risk of infection after TVL, a large prospective study has to be performed but other transvaginal needle techniques, such as ovum retrieval, carry a low risk of infection, which is estimated at 0.4% whether or not vaginal disinfection is performed (Dicker *et al*., 1993; Roest *et al*., 1996).

Operative TVL

In addition to the pure diagnostic procedure, TVL allows some operative procedures, taking advantages of the direct access to the pelvis and the internal genital organs without the need for any supplementary manipulation, the hydroflotation and the close contact with the organs. These procedures are limited to those not requiring a panoramic view of the total pelvis and are performed under general anaesthesia or sedation in a one day care centre. The fluid distension medium demands a meticulous haemostasis during the interventions, since any minor bleeding might severely impair the visualization.

The operative possibilities of TVL are still being evaluated and promising results were observed so far for PCOS and mild endometriosis and intra-peritoneal adhesions (Gordts *et al*., 2002, 2004). Other lesions must be referred to standard laparoscopy for appropriate treatment.

Conclusions

Since both the number and the age of patients with infertility is increasing, the probability of finding intra-uterine pathology in infertile patients is also increasing, which is consistent with the high incidence of intra-uterine pathology reported after several IVF failures (Oliveira *et al*., 2003). This indicates the necessity to revisit the time and form for evaluating the uterine factor. The characteristics of modern hysteroscopy (mini-instruments, atraumatic technique and fluid distension medium) (Nagele *et al*., 1996; Bettocchi and Selvaggi, 1997; Campo *et al*., 1999a, b, 2005) makes the technique a suitable first-line office diagnostic procedure for the investigation of the infertile patients, and permits to conclude that it is unacceptable not to implement the diagnostic hysteroscopy in the routine exploration of the infertile patient.

Due to the close vision and the hydro-flotation principle TVL allows detailed examination of the reproductive organs in their natural position and full evaluation of the tubal factor (salpingoscopy and patency test). In the absence of contraindications it can be offered as a first-line diagnostic procedure since it is better predictor of future fertility than HSG.

Both hysteroscopy and TVL allows the detection of major and minor lesions that can cause or contribute to the infertility, or at least impairs the results of ART treatments. Major lesions diagnosed at hysteroscopy can be treated in the same ambulatory setting or referred to the operating room, depending on the characteristics of the pathology and the patient and on the facilities available. The clinical significance of the minor lesions detected at hysteroscopy is still unclear and under evaluation and therefore no systematic treatment can be proposed.

In conclusion, the available data indicate that an endoscopy-based model has a major role and is feasible for the management of infertility. This role is even more important in developing countries where the vast majority of the population is younger than in developed countries and with limited access to ART and where the incidence of surgical pathologies, such as hydrosalpinx and myomas, is higher. Since endoscopic surgery demands specific skills that are usually not acquired during the residence programme in Obstetrics and Gynaecology, the establishment of standardized training programme for endoscopic surgery, at least for the diagnostic procedures, in the frame of a general training system for all aspects related with the management of infertility, will greatly benefit patients and society.

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