The assessment of tubal functional status by tubal perfusion pressure measurements

Vishvanath C. Karande¹, Donna E. Pratt and Norbert Gleicher

Division of GynecoRadiology, Center for Human Reproduction and the Foundation for Reproductive Medicine, 750 New Orleans Street, Chicago, IL 60610, USA

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The measurement of tubal perfusion pressures (TPP) is a recent advance in the field of gynaecoradiology. Measurement of TPP involves a standardized technique using transcervically placed tubal catheters which is reviewed in detail. TPP assesses the functional status of the Fallopian tubes, i.e. their ability to permit pregnancy. Infertile patients with normal TPP demonstrated a higher pregnancy rate (10 out of 23) than patients with elevated TPP (four out of 24, \( P < 0.05 \)). Analysis of patients who had undergone a laparoscopy as well as measurement of TPP suggest that elevated TPP are highly indicative of tubal endometriosis. Tubal catheterization with wireguides was successful in reducing mildly elevated TPP. The impact of this procedure on pregnancy rates is not known. The use of the gynaecoradiological techniques discussed in this paper has reduced the need for diagnostic laparoscopy at our centre by >60%. This was achieved without compromise in pregnancy rates and has resulted in a considerable reduction in cost.

Key words: selective salpingography/tubal perfusion pressures/tubal catheterization

Introduction

During an infertility workup, Fallopian tube function is usually evaluated only by determination of tubal patency, and/or by direct visualization of the tubes during laparoscopy (Maguiness et al., 1992). Commonly used tests for the assessment of tubal patency include hysterosalpingography (HSG) (Rubin, 1920; Maguiness et al., 1992), transcervical sonosalpingography (Richman et al., 1984), and endoscopically-guided procedures (Musich and Behrman, 1982; Brosens et al., 1987; Kerin et al., 1990; Pearlstone et al., 1992). Laparoscopy alone or in combination with other endoscopic techniques can evaluate the gross appearance of Fallopian tubes as well as their patency (Musich and Behrman, 1982; Brosens et al., 1987; Kerin et al., 1990; Pearlstone et al., 1992). Whereas each of the above mentioned techniques has advantages and disadvantages (Maguiness et al., 1992), they are all generally rather limited in their ability to assess the functional status of the tube, i.e. to predict the ability of the tube to permit pregnancy.

Two recent developments in gynaecoradiology have been recognized as facilitating both the diagnostic and the therapeutic approach towards the Fallopian tube (Gleicher et al., 1992a). The first is the replacement of spot-film HSG by a digitized radiology system that permits online documentation of flow, replay from memory and offers digitized enhancement features, similar to those used by vascular and cardiac laboratories (Gleicher et al., 1992b, Figure 1). The second development of significance is the recently developed ability to approach Fallopian tubes transvaginally utilizing catheters that are inserted transcervically through tubal ostia into the tubal lumen (Risquez and Confino, 1993). In this review, we summarize a third recent development in the field of gynaecoradiology, which we feel permits the first truly functional assessment of tubal status (Karande et al., 1995a). It involves a standardized technique used during routine gynaecoradiological procedures at our centre that assesses tubal perfusion pressures (TPP) using transcervically placed tubal catheters. In utilizing this technique, we have furthermore determined that abnormally elevated TPP do in fact correlate with tubal function, i.e. the occurrence of pregnancy.

¹To whom correspondence should be addressed
Gynaecoradiological technique

All radiological procedures at the Center for Human Reproduction are performed with a fully digitized C-arm system (OEC-Diasonics Series 9400; OEC Medical Systems Inc., Salt Lake City, Utah, USA). The X-ray image generated by the C-arm is converted to a fluoroscopic video image by an image intensifier and TV camera. The fluoroscopic image is digitized and viewed live, or processed to enhance features of interest. The digitized image can be saved on a hard disk and later recalled. In the fluoroscopic mode, images can also be stored in video format on a video cassette recorder. Post-processing can be performed on previously recorded images. This includes the ability to focus on a portion of an image (e.g. on one of the Fallopian tubes) and also contrast enhancement which helps to better delineate abnormalities (e.g. a filling defect in the uterine cavity). A recorded procedure can be played back and processed in a manner similar to the processing of an original live image. This allows for a resultant documentation of even the most subtle uterine abnormalities or most detailed aspects of tubal opacification, such as symmetry of fill, speed of tubal fill, tubal contour and pattern of spill (Karande et al., 1995a). Relevant frames can subsequently be printed out on heat sensitive paper (Fujifilm Thermal Imaging System FTI-500, Fuji, Japan).

Tubal perfusion pressure (TPP)

The technique of measuring TPP involves the injection of contrast during selective salpingography (SS) using a standardized and fully computerized system to record and document pressure curves. Briefly, a double balloon HSG catheter (Uterine cannula; Bard Reproductive Systems, Tewksbury, MA, USA) is placed in the cervix. This effectively seals the endometrial cavity. An SS catheter (Bard Reproductive Systems) is then threaded through the main channel of the HSG cannula until its tip reaches the tip of the cannula, as indicated by a marker. The distal end of the SS catheter is connected with polyethylene tubing to a preset injection pump and, by a three-way stopcock, to a pressure sensitive chip, which relays pressure information to a computer. As contrast is injected by the pump, the computer screen displays the encountered resistance in the form of a pressure curve on a screen and provides a hard copy print out. The SS catheter is thus used for HSG as well as SS. If an SS is to follow a HSG, the SS catheter is advanced into the desired cornua under fluoroscopic guidance. All studies are performed using water-soluble contrast medium (Renografin-60; Squibb Diagnostics; Princeton, NJ, USA) at a constant rate of 15 ml/min. We initially reported that 350 mm Hg of pressure is the upper limit of a normal perfusion pressure for both HSG and SS (Gleicher et al., 1992b).

Initial studies

Our initial foray into the diagnostic capabilities of TPP was encouraging (Karande et al., 1995a). In 1993, 47 women with normal HSG, by spot-film criteria, underwent bilateral SS and were subdivided into those with normal (group I, n = 23) and abnormal (group II, n = 24) TPP. Patients in both study groups underwent identical ovulation induction protocols with either gonadotrophins or clomiphene citrate, independent of pressure measurements. Clinical pregnancy rates were then recorded over the ensuing 6–10 months. Both groups were similar in aetiology of infertil-
ity, age, duration of infertility, and gravidity. Women with normal TPP demonstrated a significantly higher pregnancy rate (ten out of 23) than patients with elevated TPP (four out of 24, $P < 0.05$). Figure 2 demonstrates this fact as a life table analysis (Karande et al., 1995a).

These data seem important because they suggest that we now have a technique to evaluate the capacity of Fallopian tubes to permit pregnancy. Moreover, these data confirm the long held suspicion that tubal patency alone is unreliable as a predictor of pregnancy potential.

Only because of the ability of the equipment to record each study were we then able to review studies in a frame-by-frame manner. This allowed us to detect subtle tubal abnormalities, such as asymmetry of tubal fill, blatantly delayed opacification, or abnormal patterns of tubal spill. In fact, in an infertility population of 117 sequentially investigated females, 84% demonstrated at least one of these abnormalities (Karande et al., 1995a). If any of these abnormalities were diagnosed during HSG, selective salpingography followed, with measurement of TPP. During standard spot-film HSG, which still represents standard of care, most of these studies would probably have been considered as normal since the tubes were patent and contrast spill was observed.

Our next investigation attempted to determine the possible etiology of elevated TPP. We assessed 48 consecutive women who within a reasonably short time period had undergone an evaluation of TPP as well as a laparoscopy as part of their infertility workup (Karande et al., 1995b). Patients with laparoscopically confirmed endometriosis showed a significantly increased incidence of asymmetrical tubal filling during initial HSG (12/26, 46.1%) compared with controls (two out of 14, 14.3%, $P < 0.03$). They also demonstrated significantly more frequently (22/26, 84.6%) elevated TPP than women without disease (two out of 14, 14.3%, $P < 0.004$). Lastly, women with endometriosis also demonstrated significantly higher mean TPP than women with normal pelvises (576 ± 264 versus 450 ± 268 mm of Hg, $P < 0.05$). We therefore concluded that asymmetrical tubal filling during initial HSG and elevated TPP during SS are highly suggestive of pelvic endometriosis (Karande et al., 1995b).

Of special significance is the fact that only 14.3% of patients with a normal pelvis on laparoscopy demonstrated elevated TPP. These data provide a first evidence that endometriosis may lead to tubal disease more frequently than has been so far reported in the literature. If this assumption is correct, then tubal involvement, as reflected by high TPP, may be a principal reason for the poorly understood infertility associated with minimal and mild endometriosis. In fact, amongst endometriosis patients with elevated TPP in our study, 81% had Stage I or II disease according to the revised American Fertility Society Classification (AFS, 1985). These data thus also suggest that the assessment of TPP can not only predict the functional state of Fallopian tubes but can also greatly contribute to a presumptive diagnosis of endometriosis.

Tubal catheterization techniques have been used to treat proximal obstruction for almost a decade. Whereas initial publications focused on opening the tubes, subsequent studies analysed the resultant pregnancy rates in further detail. Motta et al. (1995) used a Jansen-Anderson Insemination Set (Cook Ob/Gyn-KJITS 552900, Indiana, USA) to perform selective salpingography in 23 patients with cornual obstruction demonstrated by hysterosalpingography. They successfully recanalized 70% of the tubes (28/40) with a subsequent pregnancy rate of 34.8% (eight out of 23). Woolcott et al. (1995) demonstrated a differential impact on the pregnancy rate of selective salpingography, tubal catheterization and wireguide recanalization in the treatment of proximal Fallopian tube obstruction. They treated 66 patients with proximal Fallopian tube obstruction (113 tubes) sequentially using selective salpingography followed, if needed, with a soft Teflon 2 French catheter and finally, if necessary, wireguided catheterization. Their success rate in opening-up the Fallopian tubes was ~90%. Wire-guide cannulation was the most effective method used to achieve tubal patency. The pregnancy rate, however, was lowest in patients that truly required wireguide cannulation (0%) in comparison with patients that achieved tubal patency with tubal catheterization (50%). Similar findings were reported by Gleicher et al. (1994) who suggested that wireguide cannulation alone is no treatment for proximal tubal obstruc-
tion. This is consistent with a hypothesis that proximal tubal disease is a continuum, with tubal obstruction of varying severity representing only one end of this spectrum. Our clinical experience (unpublished data) so far suggests that a majority of patients with tubal obstruction severe enough to require wireguide cannulation have elevated TPP.

We have attempted to reduce elevated TPP by transcervical catheterization procedures using wireguides. Such a manoeuvre is of interest since it could have potential therapeutic value by increasing pregnancy rates. In 17 patients (29 tubes) with elevated TPP, a Cope Mandril wireguide (Cook Ob/Gyn) with a diameter of 0.021 inch and length of 60 cm, was passed through the SS catheter into the tubal lumen and moved in a to-and-fro motion several times to improve upon tubal patency. TPP was re-evaluated before and immediately after tubal catheterization with the wireguide. The TPP (mean ± SD) before wireguide cannulation (779 ± 241 mm Hg) was reduced (to 474 ± 186 mm Hg) after wireguide cannulation (P <0.0001) by a mean difference of 305 ± 195 mm Hg (95% confidence interval 231–379 mm Hg). Wireguide cannulation was more effective in reducing TPP to normal in patients with mildly elevated TPP (≤600 mm Hg). In those instances, an elevated TPP appears due to a partial obstruction of the tubal lumen which can often be relieved by the catheterization procedure. In most cases of severely elevated TPP, however, wireguide cannulation will not reduce TPP to normal. In such patients it appears likely that the increased resistance to the injected fluid column is reflective of a decreased tubal compliance, as one would expect with tubal infiltration by active endometriosis or tubal wall fibrosis as a consequence of endometriosis. It is tempting to speculate that balloon dilatation of Fallopian tubes may be more effective in these patients than wire guide cannulation since it may lead to a break up of fibrotic fibres. This hypothesis could explain the reported success of transcervical balloon inflation procedures in achieving pregnancy after severe tubal occlusion (Gleicher et al., 1993).

The evidence presented here concerning tubal disease due to mild endometriosis, with resultant elevated TPP, is admittedly circumstantial. In a recent publication, Guzik et al. (1994) reported, however, a finding which conceptually supports our thesis. They found that gamete intra-Fallopian transfer (GIFT) pregnancy rates were lower in women with patent Fallopian tubes who had a primary diagnosis of endometriosis when compared with controls without endometriosis. They were unable to find a correlation between the stage of endometriosis and pregnancy rates after GIFT which once again supports the concept that tubal disease may be present even in mild cases of endometriosis. Unfortunately, pathological confirmation of this hypothesis is difficult since it is not feasible (in an infertile population) to biopsy Fallopian tubes atraumatically. It would be of interest to evaluate TPP in women undergoing hysterectomy for endometriosis. Two crucial follow-up studies are presently underway at our centre. We are presently investigating whether treatment of endometriosis with gonadotrophin-releasing hormone (GnRH) agonists and/or danazol is able to reduce elevated TPP. Concomitantly, we are addressing the question of whether TPP reduction by tubal catheterization or medical treatment of endometriosis, in fact, will increase pregnancy rates in women with endometriosis.

The complications associated with this technique are rare and no different from those reported for hysterosalpingography (infection, allergic reaction to dye). We have had no additional complications associated exclusively with the measurement of TPP.

Summary

The measurement of TPP allows for the first time a truly functional evaluation of Fallopian tubes, i.e. their ability to permit pregnancy. Elevated TPP are associated with a significant reduction in pregnancy rates even if Fallopian tubes are anatomically patent. It is likely that tubal disease due to endometriosis may have the aetiology of elevated TPP in a large majority of cases. Use of a fully digitized C-arm system, with the capacity to record gynaecoradiological contrast studies online, allows the documentation of even very subtle tubal abnormalities. The use of the gynaecoradiological techniques discussed above has reduced the need for diagnostic laparoscopy at our centre by >60%. This was achieved without compromise in pregnancy rates and has resulted in a considerable reduction in cost.

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