Radionuclide hysterosalpingography does not distinguish between fertile women, before tubal sterilization, and infertile women

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The female genital tract is capable of active transport that can be demonstrated by serial scintigraphic imaging over time (radionuclide hysterosalpingography; RN-HSG). RN-HSG has been suggested to offer a more functional approach to tubal infertility diagnosis than conventional patency tests. However, before RN-HSG can be recommended as a routine method, its reliability in showing active transport in fertile women must be demonstrated. Therefore we compared RN-HSG in two groups: 38 fertile women before tubal sterilization and 38 women undergoing infertility work-up. Tubal transport demonstrated by RN-HSG was comparably distributed in both groups and classified as bilateral (17 versus 19), unilateral (12 versus 7) or no transport (6 versus 9). In each group three RN-HSG images were not interpretable. There was no association between patency test results and RN-HSG in the two groups. Our data suggest that RN-HSG in its present form does not seem to be a reliable method for infertility work-up. Because RN-HSG and patency tests most probably measure different properties of the genital tract, the phenomenon of active particle transportation should be studied further to enable the development of a reliable tool for the investigation of tubal function.

Keywords: Fallopian tube/radionuclide hysterosalpingography/tubal infertility

Introduction

Tubal damage and pelvic adhesions are common causes of female infertility and are often related to previous pelvic inflammatory disease such as chlamydial infection (Osser et al., 1989). Subfertility of tubal origin is usually diagnosed by demonstrating impaired patency at hysterosalpingography (HSG), at laparoscopy with chromopertubation or at endovaginal ultrasonography. However, no information about the active transport capacity of the tubes can be obtained by these methods. Furthermore, HSG, the most common method, has low sensitivity in detecting tubal pathology (Mol et al., 1996).

It is well documented that the female genital tract is capable of active transport. Carbon particles have been used to demonstrate ascending transport capacity (Egli and Newton, 1961), and the female genital tract is also able to transport inert radioactively labelled material from the vagina to the ovarian surface. This migration can be recorded by serial scintigraphic imaging over time using technetium-99m human albumin microspheres (Venter and Iturralde, 1979). It has been recommended that this method, called radionuclide hysterosalpingography (RN-HSG), could be used as a complementary procedure in infertility investigations to demonstrate the functional capacity of the oviducts (Brundin et al., 1989, 1993).

Several authors have considered RN-HSG to be the method of choice to investigate a lack of active tubal transport capacity. Transport of radionuclide and spermatozoa has been suggested to be dependent on the same tubal mechanism (Venter and Iturralde, 1979; McCalley et al., 1985; Stone et al., 1985; Becker et al., 1988). For that reason, RN-HSG has been considered to be a suitable method for the investigation of tubal damage, even when routine HSG and/or laparoscopy with chromopertubation have revealed normal conditions. Much evidence supports the fact that active transport, as demonstrated by RN-HSG, is intraluminal and not lymphatic or haematogenous (Egli and Newton, 1961; Iturralde and Venter, 1981; Steck et al., 1991). However, few efforts have been made to evaluate RN-HSG in fertile women. So far only a small number of women with active tubal transport have been studied (Stone et al., 1985; Becker et al., 1988; Steck et al., 1991). To prove the reliability of RN-HSG, it is of vital importance to show whether there is a difference in active transport capacity in fertile compared with infertile women. The objective of the present prospective study was to investigate this difference.

Materials and methods

Fertile women

A total of 38 healthy women volunteered for RN-HSG before undergoing tubal sterilization. They were aged 28–44 years (mean 37.2), had experienced one to nine intrauterine pregnancies (mean 2.5) and the time from last pregnancy ranged from 1 to 15 years (mean 3.4) prior to the study. In all, 26 women underwent chromopertubation during sterilization. It was possible to evaluate images from RN-HSG in 35 women. All women continued their current contraceptive technique until tubal sterilization; 16 (46%) had used either no contraceptive or barrier methods, nine (26%) had an intrauterine device and 10 (28%) used oral contraceptives.

Infertile women

In all, 38 women with a history of infertility ranging from 1 to 23 years (mean 5.9) volunteered for RN-HSG. They were aged 25–41
years (mean 32.2). Of these infertile women, 23 were also investigated by HSG. It was possible to evaluate images from RN-HSG in 35 women.

**Timing of RN-HSG**
The aim of RN-HSG was to perform RN-HSG within 3 days prior to ovulation. The day for the examination was decided upon on the basis of menstrual data and a cervical mucus score. A wet smear was examined to minimize the risk of vaginal infection. Serum progesterone concentrations were measured at the day of RN-HSG and 1 week later to confirm the pre-ovulatory phase.

**Procedure of RN-HSG**
Albures (Solco Basle Ltd, Birsfelden, Switzerland) was used, consisting of human serum albumin particles 0.2–1.0 mm in diameter labelled with 1 ml technetium-99m to a total radioactivity of 100 MBq. A 1.0 ml syringe was filled with 0.1 ml of the solution, which gave a nominal radioactivity of 10 MBq. An Aspiglaire tube (Aspiglaire, IMV, L’Aigle, France) was then filled with the solution in the syringe. The radionuclide solution was deposited with the Aspiglaire inside the internal cervical os, with the woman in a recumbent position. The intrauterine position of the radionuclide solution in the Aspiglaire tip was first confirmed on the screen of a γ-camera (Starcam Mobile 300 A; General Electric Medical Systems Europe, London, UK) equipped with a pinhole collimator. After deposition of the radionuclide, a dynamic acquisition was started with 5 s/frame for 10 min, followed by 60 s/frame for 20 min and a static acquisition of 200 000 counts or a total acquisition time of 40 min with the woman in a plane supine position. Another static acquisition was performed at 3 h and sometimes at 5 h after deposition. The women were allowed to move about freely between measurements. Documentation of the images was made on transparent film.

**Interpretation**
The images were classified into three main groups: transport, no transport and not interpretable (Figure 1). These were defined as:
- **Transport**: images that showed unilateral or bilateral tubal transport from the uterine cavity;
- **No transport**: images that showed a clearly outlined uterine cavity and lacked lateral activity;
- **Not interpretable**: images that showed an unclearly outlined uterine cavity and lacked lateral activity.

**Statistics**
Statistical analyses were carried out with Fisher’s exact test for group comparison. A probability value of $P < 0.05$ was considered to be statistically significant.

**Ethical aspects**
The study was approved by the Local Ethics Committee of the Karolinska Hospital (Stockholm, Sweden) and by the local Radiation Protection Committee of Danderyd Hospital (Sweden).

**Results**
The outcome of RN-HSG transport in fertile and infertile women is summarized in Table I. There were no statistically significant differences between the groups. Unilateral, bilateral and no transport were represented in both groups.

Peroperative chromopertubation was performed in 26 fertile women (Figure 2). The results were compared with RN-HSG. Of 9 women with bilateral patency at chromopertubation, seven showed unilateral and nine bilateral active RN-HSG transport. Three women had no active transport capacity and this small subgroup was not different in terms of age, number of pregnancies, time elapsed since last pregnancy or time of the examination compared with those women with active transport. One woman had no patency when peroperative chromopertubation was performed. No differences were found in terms of RN-HSG transport in women who had used contraceptive methods involving intrauterine devices, oral contraceptives or the barrier method (Table II).

In all, 23 infertile women were investigated with traditional
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Figure 2. Peroperative chromopertubation was performed in 26 fertile women and the results were compared with those obtained following radionuclide hysterosalpingography.

Figure 3. In all, 23 infertile women were investigated with traditional hysterosalpingography and the results compared with those obtained following radionuclide hysterosalpingography.

Table II. Radionuclide hysterosalpingography results in relation to contraceptive method in the fertile group

<table>
<thead>
<tr>
<th>Method</th>
<th>Bilateral transport</th>
<th>Unilateral transport</th>
<th>No transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrier method</td>
<td>6</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Intrauterine device</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Oral contraceptive</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

HSG. A comparison with RN-HSG is shown in Figure 3. A total of 10 women showed bilateral passage of contrast media on HSG, of whom seven had bilateral and one unilateral active transport on RN-HSG. Two women showed bilateral patent tubes at HSG but no active transport of radionuclide; both had undergone legal abortions 8 and 12 years ago respectively, after which one had experienced a history of abdominal surgery caused by a ruptured appendix and one had suffered from pelvic inflammatory disease.

It became apparent that our timing of RN-HSG using mucus score and menstrual data was inaccurate. In some women serum progesterone concentrations on the day of RN-HSG and 1 week later showed that RN-HSG was performed in three different phases of the menstrual cycle and that differences in tubal transport were not correlated to cycle phase. The 10 women who did not ovulate, because they had used oral contraceptives, had results similar to women who did ovulate. We found no evidence that smoking (Figure 4) or net deposited radioactivity in the uterine cavity was related to tubal transport. In addition, the histological examination of specimens from the middle portion of the tube at sterilization revealed no correlation to lack of transport.

Discussion

Several authors have suggested that RN-HSG could be used in clinical practice as a means of diagnosing a damaged tube even if it appeared to be normal according to current investigation techniques including HSG and chromo-perpertubation. This was based on the theory that a lack of particle migration should demonstrate damage to cilia or impaired tubal muscular activity, and hence impairment of normal tubal function. Consequently, fertile women should exhibit normal RN-HSG images.

In our study, bilateral, unilateral and no transport, observed in both the fertile and infertile groups, were comparably distributed. The patency tests also showed all combinations of tubal patency in both groups. Moreover, there was no association between patency test outcome and RN-HSG pattern in the two groups. Women with bilateral and unilateral patency had bilateral, unilateral or no transport as demonstrated with
RN-HSG. The obvious lack of a relationship between RN-HSG pattern and patency test results could imply that the two methods measure different properties of the female genital tract, especially of the Fallopian tubes. Because our study did not reveal any difference in active tubal transport between the fertile and infertile groups, our data do not enable us to claim that RN-HSG results could be related to fertility potential.

Kuntz et al. (1996) showed in the early, mid- and late follicular phases of the cycle a pattern of increasing distribution of radioactivity into the Fallopian tube ipsilateral to the dominant follicle. In our study we have data concerning the side of the pre-ovulatory follicle only in 11 women which do not confirm the observation by Kuntz et al. Among six women with bilateral RN-HSG transport, only three had a follicle >17 mm in diameter. Four women with unilateral transport and one without transport all had follicles <17 mm in diameter. We do not regard our data to be conclusive because the number of women investigated was too small. However, the suggestion of Kuntz et al. (1996), that directed ascension of radionuclide towards the dominant follicle is a specific utero-tubal function controlled hormonally by the dominant follicle, is contradicted by our observation that 10 women using combined oral contraceptives, and consequently with no dominant follicle, all showed active tubal transport.

Because HSG and laparoscopy with chromopertubation provide no information about the physiological function of the oviducts, the development of methods demonstrating this function would be of high clinical value. The phenomenon of radionuclide transport needs further clarification before it can be introduced as a clinical investigation tool. Would it be possible with RN-HSG to visualize tubal transport operating from the distal part to the uterine cavity? Decker and Decker (1954) described this phenomenon by depositing starch particles in the pouch of Douglas. However, their study has not been confirmed.

In conclusion, the RN-HSG images were not consistent with tubal patency results. Moreover, RN-HSG could not distinguish between a fertile and an infertile group of women. Thus, RN-HSG does not seem to be a reliable method for infertility work-up and should not be used as a clinical routine method. However, phenomena of active particle transport should be studied further so as to develop a reliable tool for the investigation of tubal function.

References