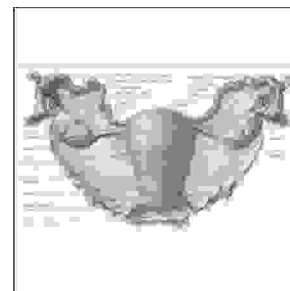


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FEMALE INFERTILITY; COMPARISON OF HYSTEOSALPINGOSCINTIGRAPHY (HSSG) AND LAPAROSCOPY.



DR. KALSOOM AKHTAR

M.Sc (Nuclear Medicine),
Medical Officer (BINO).

DR. MOHAMMAD ANEES

M.Sc (Nuclear Medicine),
Senior Medical Officer (BINO).

DR. NAEEM AHMED LAGHARI

DMRT, MCPS (Radiotherapy),
Consultant Oncologist and Director BINO.

Dr. Mohammad Iftikhar Alam

M. Sc (Nuclear Medicine),
Senior Medical Officer (BINO).

Dr. Farzana Kousar,

M. Sc (Nuclear Medicine),
Medical Officer (BINO).
Bahawalpur Institute of Nuclear Medicine
& Oncology (BINO), Bahawalpur,
Pakistan.

ABSTRACT... bino@mul.paknet.com.pk **Objective:** The main objective of this study was to see the role of Hysterosalpingoscintigraphy (HSSG) in the evaluation of fallopian tube patency and function and its comparison with Laparoscopy. **Design:** Comparative Study. **Place and Duration of Study:** The study was conducted at Bahawalpur Institute of Nuclear Medicine and Radiotherapy, Bahawalpur during a period of 6 months from 1st March to 31st August 2005. **Material and Methods:** Static HSSG was performed after instillation of 4mCi ^{99m}Tc-MAA in posterior vaginal fornix in 40 patients. Images were taken at an interval of 1hr, 2hrs, 3hrs anteriorly in supine position. **Results:** Out of 40 patients, 20 patients had bilateral blocked tubes, 13 patients had bilateral patent tubes, 4 patients had blocked left tube and 3 patients had blocked right tube. The calculated Sensitivity, Specificity, PPV and NPV for HSSG was 90%, 85%, 90% and 90%. The agreement between Laparoscopy and HSSG was found in 36 out of 40 patients. **Conclusions:** This simple procedure can play an important role in the evaluation of infertility, especially in patients who suffer from unexplained infertility due to a tubal factor. It was also concluded that HSSG be accepted with the other correlative imaging procedures, on a routine basis in work up of infertile females.

Key words: Hysterosalpingoscintigraphy, Laparoscopy, 99m Tc-MAA.

INTRODUCTION

The desire of a women for children is sometimes stronger than self-interest in beauty and figure, and may

be stronger than the claims of a career. Childlessness may be a tragedy to the married woman, and can be a cause of a marital upset as well as of personal

unhappiness and ill health¹. Infertility is an extremely isolating experience and according to American Association of Reproductive Medicine it affects about 6.1 Millions or 10% of reproductive age population². HSSG was introduced by Iturralde and Venter in 1981³, modified by Becker and coworkers in 1988⁴, by Kunz G 1996⁵ and by Wildt and colleagues in 1998⁶. HSSG is the simple and accurate method of evaluating fallopian tube patency and shows the ascent of activity in cervix, uterus and fallopian tubes. Upon ejaculation into the anterior vagina the pool of highly concentrated semen bathes the external cervical os and spermatozoa gain access to the mucus-filled cervical canal largely under the influence of their own motility. Migration of spermatozoa through the uterus to the fallopian tubes depends on the contraction of uterus while motility of sperm maintains the spermatozoa in suspension in uterus fluids, prevents their adhesion within the uterus⁷.

HSSG is used as an additional diagnostic method of evaluating tubal patency or function in infertile females. Albumin microspheres, with a 95% mean diameter of 5-40 μ m are label with technetium-99m and suspend in normal saline for 5 min prior to application. A 0.5 ml aliquot of the suspension containing label albumin particles with a radioactivity of 148 MBq with <0.1% free technetium is placed by a syringe into the posterior vaginal fornix with the patient in the supine position, which is not changed during the whole procedure. Serial anterior scintigrams are performed with a gamma camera (Orbiter; Siemens) over 1hr, 2hrs, 3hrs and if needed at 24hrs, starting 1 hr after application of the suspension.

For the assessment of the ascent of the labeled microspheres, the genital tract was subdivided into three compartments: the upper vagina, the place of application, was compartment 1, and the uterine cavity and the isthmic part of the tubes were compartments 2 and 3 respectively. In all patients the localization of the dominant follicle was documented, whenever possible. Thus, in the assessment of the ascent into compartment 3, transport into the right or left or into the tube ipsi- or contra-lateral to the dominant follicle was distinguished.

The ampullary part of the tubes and the peritoneal cavity were designated compartment 4^{5,8}. Because it was, in general, difficult to distinguish clearly between compartments 3 and 4, data from these two compartments were combined in the quantitative assessment of transport beyond the confines of the uterine cavity. The tubal patency tests are avoided during menstruations, after the curettage with recent H/O active salpingitis, when there is suspicion of active tuberculosis of the genital tract and when there is evidence of the infection of the lower genital tract, such as a purulent discharge.

A lot of work has been done on various aspects of HSSG like tubal transport velocity determination with dynamic HSSG⁹, Sperm transport in the human female genital tract¹⁰, Estimation of anatomical aspect of oviducts after reconstructive operations involving fallopian tubes¹¹, Uterine contractility, directed sperm transport and intrauterine pressure measurement, uterine hyperperistalsis and dysperistalsis as a dysfunction of the mechanism of rapid sperm transport in patients with endometriosis and infertility. It is a simple and accurate method of evaluating fallopian tube patency¹².

There are many advantages of this procedure such as it is a simple and safe technique, radiation exposure is less than HSG, Non-invasive procedure had sensitivity and specificity of more than 90%. But this procedure had some disadvantages such as it is lengthy procedure, costly and not easily available at present but with passage of time it may be available in most nuclear

medicine departments¹³. While Laparoscopy required general anesthesia.

MATERIAL AND METHODS

HSSG was performed to assess the patency and function of fallopian tubes in 40 patients. All females of child-bearing age fulfilled the inclusion criteria and were selected for further analysis, and all of them had a negative pregnancy test. All pregnant females and patients with recent history of salpingitis or other infections were excluded from the study.

After taking the informed written consent procedure was explained to the patient and protocol was discussed with the Supervisor and Gynecologist involved. On the basis of clinical assessment, hormonal profile, Ultrasonographic and laparoscopic findings the patients were scheduled for Tc-99m labeled MAA scan (Hysterosalpingoscintigraphy) on different days.

All scans were done on a SIEMENS gamma camera system with parallel holes Low Energy All Purpose (LEAP) collimator. Static views were taken at 1hr, 2hrs, 3hrs and if needed at 24hrs. Data was acquired for 300Sec. The performance of the gamma camera was assessed by various quality control procedures. Background counting, uniformity checks using Co-57 flood source and peaking of the camera for Tc-99m were performed daily while linearity and resolution checks using line and bar phantom were performed weekly.

The Radiopharmaceutical used in performing the study was ^{99m}Tc -labeled Macroaggregated albumen (^{99m}Tc -MAA) with the commercial name of MAASOL was received from Radioisotope Production Group, Amersham, SORIN S.r.i. Italy. The agents were predispensed, freeze-dried sterile ingredients which when reconstituted with Tc-99m elute produced in a sterile solution. Sodium pertechnetate (NaTcO_4) was obtained from the Pakjen Tc-99m Sterile Generator provided by PINSTECH Islamabad. The generator contained fission-product molybdenum-99 (Mo-99) adsorbed on alumina column shielded by lead. The column was attached to reservoir of sterile pyrogen free normal saline. Activity was eluted aseptically using sterile evacuated elution vials.

After taking the informed consent the patient was placed in lithotomy position. Clothes were removed and patient was covered with a sheet. The genitalia cleaned with pyodine solution. Sim'S Speculum was inserted in vagina and lips of cervix were held with the help of sponge holder to clearly visualize the posterior fornix. A dose of 148MBq (4mCi) was placed in the posterior fornix with the help of syringe without needle. The genitalia were covered with sanitary pads to prevent the spillage of activity. After removing the legs from the lithotomy table

and placing her on the bed in supine position and the patient was asked to stay in that position for 3 hours. The scans were done after 1, 2, 3 and if needed at 24 hrs of insertion of the radio-pharmaceutical.

Scans were interpreted as abnormal if there was no activity in one or both tubes and especially if the distal focal area of high activity in the fimbriae did not show up to 3 hours after deposition. The course and migration of ^{99m}Tc -MAA by the propulsive action of the tubal ciliary's mechanism during the HSSG was expressed as the transit time from the deposition in the vagina until appearance of activity in either fimbriae. In healthy females with patent tubes the transit time varies from 1 to 3 hours.

Statistical analysis was done by calculating the sensitivity, specificity, positive predictive values, negative predictive value for all images of HSSG. Chi-square test was used to see the significance level. The p value obtained from this study by applying the Chi-square test is <0.0001 . A value of 0.05 was considered statistically significant and p-value of 0.01 was considered statistically highly significant.

RESULTS

The study group consisted of forty patients. Most of the patients were between the ages of 18-35 years and few patients were between the ages of 35-45. Out of these forty patients, twenty-six had normal menstruation, ten had irregular menstruation but normal hormonal profile while four had no menstruation with normal hormonal profile.

Out of 40 patients, twenty five had history of infertility of more than five years, out of these fifteen patients were those who presented with secondary infertility and ten patients presented with primary infertility. While fifteen patients were those who had history of infertility of less than five years and all of them presented with primary infertility and results were compared with Laparoscopy. The agreement and disagreement between two modalities were summarized in (Table I). All of these patients had negative pregnancy test. The patients with

normal menstruation were asked to come on 5th day after stoppage of menses while patients with irregular menses and no menses were planned to do study on the same day.

Results	No. Of patients
Concordance between HSSG and Laparoscopy	36
Discordance between HSSG and Laparoscopy	04

This procedure can be performed by using ^{99m}Tc-MAA, ^{99m}Tc-DTPA and ^{99m}Tc-HAM. ^{99m}Tc-MAA is most widely used because, although the ^{99m}Tc-MAA molecules differ biochemically and immunologically from human spermatozoa, their diameter roughly approximates the size of the human spermatozoa. It has been suggested that the radio-labeled tracer molecules are transported by the same mechanism that were originally designed for support of spermatozoal migration.

Regarding the pattern of images obtained with this procedure on a gamma camera there was a central elongated area of the high activity over the vagina. Directly on the top of this area appeared a narrow stretch of activity corresponding to the endo cervix. The uterus appeared as a small area of high activity of varying size and shape but the most commonly the uterus appeared as triangular area of increased activity due to impression of bladder.

The tubes were seen extending laterally with a distal hot spot of high activity corresponding to the fimbriae. In some cases activity in the region of the tubal isthmus could not be visualized although there was high activity in their distal segment. In most cases activity progressed within the first hour simultaneously through both tubes, while in others activity moved faster in one tube than in the other showing increased activity on one side. Transport was directed predominantly into the tube ipsilateral to the ovary bearing the dominant follicle; the

contra-lateral oviduct appeared to be functionally closed. The proportion of patients exhibiting ipsi-lateral transport did increase concomitant with the increase of the dominant follicle and rapid sperm transport occur as the follicular phase progress^{6,10,11,12,13}. The disadvantages of this procedure are that it is lengthy, costly and not easily available at present but with passage of time it may be available in most nuclear medicine departments. The Scans obtained during the study were shown in [Figure 1-3].

Results obtained from HSSG are shown in [Table II].

Results	No. Of patients
Bilateral blocked tubes	20
Bilateral patent tubes	13
Left tube blocked	04
Right tube blocked	03

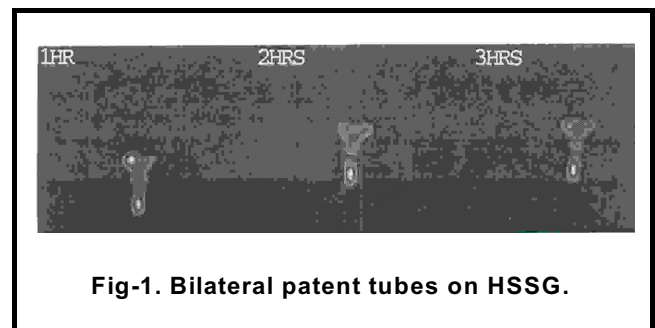


Fig-1. Bilateral patent tubes on HSSG.

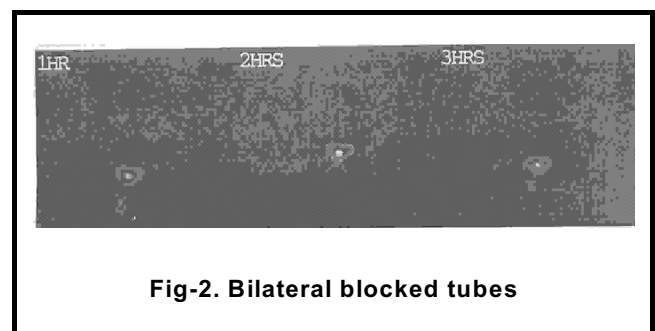


Fig-2. Bilateral blocked tubes

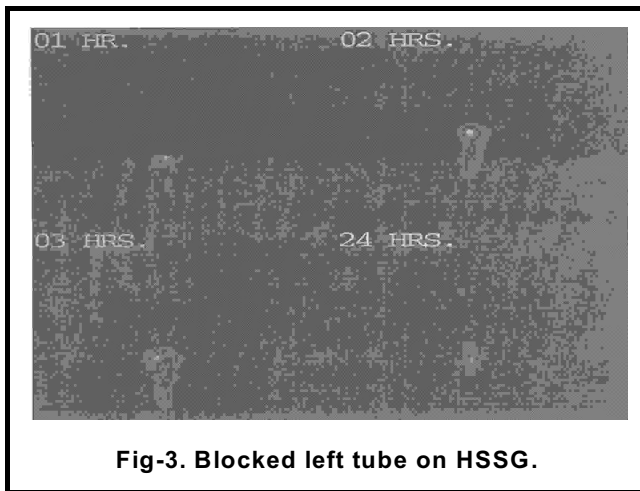


Fig-3. Blocked left tube on HSSG.

DISCUSSION

A number of studies suggest that the rapid ascent of spermatozoas within the female genital tract to the site of fertilization is not dependent upon motility of the spermatozoa, but appears to be directed by the anatomical and functional unit of the uterus and fallopian tube. In fact, sperm transport is based on directed uterine peristalsis and myometrial contractions towards the ovary bearing the dominant follicle⁶. In most cases activity progressed within the first hour simultaneously through both tubes, while in others activity moved faster in one tube than in the other showing increased activity on one side. Transport was directed predominantly into the tube ipsilateral to the ovary bearing the dominant follicle, the contralateral oviduct appeared to be functionally closed.

In this study six patients presented with unilateral blocked on HSSG but patent on Laparoscopy. These patients were those in whom the scans were done in follicular phase and there was unilateral blocked then these patients were asked for USG to see the dominant follicle and was confirmed by doing Laparoscopy as if tubes were patent on Laparoscopy then these patients were considered normal with patent tubes which were otherwise blocked on HSSG. It was also proved from the study that the absence of transport into the fallopian tubes is associated with a very low probability of becoming pregnant spontaneously, even in the presence of patent tubes on Laparoscopy^{5,6,10}. Comparing with the

Laparoscopy the procedure yielded comparable results in females with patent or clearly obstructed tubes. Barrada et al with other investigators found once again that none of the patients showing bilateral dysfunction on HSSG became pregnant, even if the fallopian tubes had shown patency on Laparoscopy^{12,14}.

Uszler et al. reported on a series of 46 infertile patients, that no patient whose tubes were non-functional on HSSG became pregnant without IVF, and five live, healthy births resulted in patients showing function of at least one tube. Uszler stated that HSSG is the only method to visualize fallopian tubal function, and it can aid in infertility evaluation¹⁵. Radiation dose to the ovaries from HSSG is only 11% of the radiation dose from HSG. The radiation dose can further be reduced by reducing the injected dose or by placing the radiotracer in the uterine cavity¹⁶. McCalley et al. have estimated an ovarian dose of 0.75mGy/MBq (1.8rad/mCi) for HSSG, assuming that 5% of the administration dose resides on each ovary for the duration of the physical decay of Tc-99m¹⁷. Stabin corrected this dose estimate, suggesting that the actual dose to each ovary is 1.5mGy/MBq¹⁸. Kennedy et al. estimate the dose to be much lower because the maximum dose in the ovaries was found to be 4.6% of the administered activity, giving a maximum dose of 2.35mGy per ovary¹⁹. Using ^{99m}Tc-pertehnetate, Yang et al. reported a dose of 1.08mGy (108mrad) per study²⁰. All these investigators calculated the dose by different method but total dose calculated by each investigator was 5% of the total dose.

Two patients presented with secondary infertility and when HSSG was done in these patients the tubes were blocked but on Laparoscopy a large filling defect was found in the uterine cavity. On USG there were large fibroids approaching the opening of fallopian tubes that caused the distortion of pelvis and thus blocked tubes and the cause of infertility in these patients.

Stuart Campbell and Ash Monga studied that when fibroids are located near fallopian tubes they tend to cause infertility. Cornual fibroids block the opening of tubes causing sterility and are also difficult to rectify.

Multiple fibroids also can cause infertility. Intramural fibroids are those that are located close to the fallopian tubes and cause infertility. These are more difficult to treat due to their location and surgery is risky as it may further affect the tubes, which are very small and delicate [21]. When HSSG was compared with Laparoscopy, HSSG showed sensitivity of 90% and a specificity of 85%. The Positive and Negative predictive values of the test were 90% and 90%. This is comparable with other studies done by Iturralde and Venture [22]. The reported sensitivity, Specificity, PPV and NPV for HSSG are 93%, 94%, 97% and 90%.

As far as radionuclide-imaging process is concerned it was encouraging to find a close correlation of this procedure when compared with Laparoscopy. However most important of all is the fact that HSSG reflects the functional state of the female reproductive system by showing particulate migration, which is not the case of the other anatomically dependent diagnostic modalities used to evaluate tubal patency. It was found that in two cases; Laparoscopy was showing anatomical tubal patency only because both the contrast media and the dye were injected under extreme pressure, opening kinked tubes that under other circumstances would not be patent. HSSG proved in these two patients that there was no migration of ^{99m}Tc -MAA through the fallopian tubes, this being the probable cause for their infertility¹³.

In two patients, where blockage was diagnosed on the radionuclide test but patency found on Laparoscopy a higher prevalence of pelvic abnormality was found and in follow-up period these patients did not conceive even after reconstructive procedure. In one patient where tubes were patent on HSSG but blocked on Laparoscopy, the patient became pregnant within 4 months of the test. This is probably due to the forced injection of relatively large volumes of fluid, which does not occur with the radionuclide test and may explain the finding of radionuclide patency in one patient with apparent blockage of anatomically normal tubes on Laparoscopy. Comparing with Laparoscopy, HSSG is a simple, safe, convenient and non-invasive technique while Laparoscopy is an invasive procedure, required

general anesthesia and there are more chances of complications.

A similar study conducted by Steck et al. who reported congruent findings between tubal patency on Laparoscopy and tubal migration on HSSG in 23 out of 28 patients, with an overall correlation of 61%. When bilateral patency was reported on Laparoscopy, correlation with HSSG results was 18/27(67%). But scans were reported as bilaterally abnormal in the remaining five patients. As expected, HSSG imaging showed no tubal migration of the tracer in all three individuals with anatomical blockage on Laparoscopy.

Due to the functional superiority of HSSG over Laparoscopy the Gynecologists may be willing to change the superior spatial resolution of Laparoscopy if the functional nature of HSSG could be shown to predict outcome better. Technical refinements can be introduced to improve the imaging quality, reduce the radiation dose and increase awareness of the study on part of nuclear medicine and referring physicians.

HSSG allows the investigation of tubal function with ease of performance, patient comfort, and functional relevance. The disadvantages of this procedure are that it is lengthy and not easily available at present but with passage of time it may be available in most nuclear medicine departments.

It is also clear from the study done by Steck T and colleagues that the Comparison between HSSG and Laparoscopy may seem inadequate as the nature of the procedure differs fundamentally, but at present there is no other method in use that can reveal actual tubal function.

CONCLUSIONS

It is concluded that HSSG although a relatively new technique but it is the simple and accurate method for evaluation of fallopian tube patency and function in infertile females. It is also only non-invasive procedure for visualizing and evaluating in vivo the ciliary transportation capacity of the luminal epithelium lining of

the inaccessible fallopian tubes. This simple procedure can play an important role in the evaluation of infertility, especially in patients who suffer from unexplained infertility due to a tubal factor. It is also concluded that Hysterosalpingoscintigraphy be accepted with the other correlative imaging procedures, on a routine basis as part of the investigation of infertile women.

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It is God who makes women
beautiful;
it is devil who makes her
pretty.

Victor Hugo