Long-term fertility prognosis following selective salpingography and tubal catheterization in women with proximal tubal blockage

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BACKGROUND: The possibility of conception following selective salpingography and tubal catheterization is believed to decline sharply a few months after the procedure. This observation may be due to the relatively small number of patients and short follow-up of previous studies. Furthermore, couples with other causes of infertility apart from proximal tubal blockage have usually been excluded. METHODS: Survival analysis of conceptions of 218 consecutive infertile women with proximal tubal blockage who underwent selective salpingography and tubal catheterization was performed. There were no exclusion criteria. Follow-up ranged from 16 to 56 months. RESULTS: A total of 47.2% of spontaneous conceptions and 43.2% of all conceptions, apart from those achieved by IVF or ICSI treatments, occurred after the first 12 months following selective salpingography and tubal catheterization. The decline in the possibility of pregnancy during the study period (conception hazard rate) was only minimal. CONCLUSIONS: In a population of infertile women with proximal tubal blockage, a significant proportion of conceptions occur after the first 12 months following selective salpingography and tubal catheterization. The presence of any additional causes of infertility in the couple should not be regarded as an absolute contraindication to the procedure.

Key words: infertility/selective salpingography/survival analysis/tubal catheterization

Introduction

Selective salpingography and tubal catheterization (SS/TC) under fluoroscopic guidance is a transcervical procedure used for the diagnosis and treatment of proximal tubal blockage (PTB). Several series have established the effectiveness of SS/TC in achieving Fallopian tube recanalization and restoring fertility in women with PTB (Capitanio et al., 1991; Ferraiolo et al., 1995; Woolcott et al., 1995; Lang and Dunaway, 1996).

It has been suggested that the best chance for these women to conceive is in the first 3 months after SS/TC (Thurmond and Rosch, 1990; Darcy et al., 1991). To support this, the hypothesis that PTB reoccurs in many women shortly after SS/TC has been proposed (Lang, 1995). Probable causes could be recurring retention of debris in the proximal tube or Fallopian tube scarring. However, this hypothesis is not supported by data about tubal patency rates at follow-up hysterosalpingograms (HSGs) after SS/TC. Tubal patency is maintained in 63–88% of women who did not conceive 3–6 months after SS/TC (Kumpe et al., 1990).

On the other hand, in most published series, the number of women included is relatively small and they were followed-up for relatively short periods. In a detailed review of the management of PTB published in 1999, nine SS/TC studies were included (Honore et al., 1999). The mean number of women included in each was 54. When clearly reported, mean follow-up in these studies was 12 months. Therefore, the suggestion that the possibility of conception appears to diminish a few months after the procedure may be the result of inadequate follow-up of insufficiently large cohorts of patients. The probability of conception as a function of time since SS/TC (conception hazard rate) has not so far been examined.

Furthermore, the presence in a couple of any infertility factors in addition to PTB has been an exclusion criterion for most reported series of SS/TC. Therefore, information about the results of the procedure is mainly derived from the study of ‘ideal populations’, and thus is not reflective of practice in a routine clinical environment.

The aim of the present study is to provide information about the longer-term (after the first 12 months) fertility prognosis of women diagnosed with PTB following SS/TC and to report
on the conception hazard rate after the procedure. We studied a heterogeneous population of consecutive infertile women, with only the diagnosis of unilateral or bilateral PTB in common. Live birth rates are reported.

Materials and methods

Patients
In a 3 year period starting April 1996, 231 SS/TCs for the management of women diagnosed with PTB were attempted at the Assisted Conception Unit, Birmingham Women’s Hospital, a tertiary teaching reproductive medicine department. The procedure was completed in 226 cases (97.8%). In five cases the procedure was not completed for the following reasons: one woman decided not to proceed on the day of the procedure because of anxiety and fear of pain, another could not tolerate the passage of the speculum and asked for the procedure to be terminated, in a third case it was impossible to advance the SS catheter as the cervical os was found to be too tight, one patient experienced a vasovagal attack during the insertion of the SS catheter, and in another there was significant intavasation of contrast medium in the early stages of the procedure, which was then abandoned.

Reproductive outcome was assessed with semi-structured questionnaires sent to women along with prepaid reply envelopes in August 2000. In January 2001 a second mailshot was sent to patients who had not previously responded. An effort was made to contact subjects whose responses were unclear or incomplete as well as non-responders, by telephone. If the telephone numbers available in the patient’s case notes were inaccurate, their family doctor or the health authority was contacted in order to try to identify the patient’s current phone number.

Five women had SS/TC performed twice during the study period. Only the first procedure was included in the study. Three cases were excluded from the analysis. One woman had SS/TC in order to confirm successful sterilization, another had a hysterectomy during the follow-up period, and a third indicated that, due to changes in her personal circumstances, she had stopped trying to conceive a few months after SS/TC.

Therefore 218 cases were included in the analysis. The average age (± SD) of the women included in the analysis was 32.6 (± 5.1) years and the median duration of infertility was 43 months (range 5–281). Of them, 77 (35.3%) presented with primary and 118 (54.1%) with secondary infertility [information missing in 23 (10.6%) cases]. The diagnosis of PTB was made on HSG in 105 cases (48.2%), on laparoscopy and dye test in 50 (22.9%) and with both tests in 63 (28.9%) cases. If a discrepancy between the HSG and laparoscopy and dye test results was found, then the laparoscopy findings were accepted. It was possible to determine whether bilateral or unilateral PTB had been diagnosed before SS/TC in 154 (70.6%) of the cases, of whom 76 (49.3%) had bilateral and 78 (50.7%) unilateral PTB.

Nine women had undergone a salpingectomy (right in four cases and left in five). In five women, SS/TC was performed after sterilization reversal surgery and in six after tubal surgery (cornual resection–reanastomosis for PTB in one case and salpingostomy for distal blockage in three cases, while information for the nature of the tubal surgery could not be identified in two cases). One woman had laser ablation of a uterine septum, one was diagnosed with a unicornuate uterus and two women had myomectomies before. Endometriosis (all stages) was laparoscopically confirmed in 16 (7.3%) women, anovulation was diagnosed in 25 (11.4%) cases (information missing in 61 cases), and male factor, using the World Health Organization definitions (World Health Organization, 1999), was present in 32 (14.6%) of the couples (information missing in 77 cases).

Statistical methods

Only the woman’s first conception during the study period was considered. Cumulative conception rates and conception hazard rates were obtained from Kaplan–Meier survival analysis. Smooth estimates of these rates were obtained from Weibull analysis (Collett, 1994). StatView Version 5 software (SAS Institute Inc., 1998) was used for statistical analysis.

On an initial analysis, only spontaneous conceptions were counted as successes. Conceptions arising after medical intervention were considered as censored at the time of conception. Cases for whom no conception was reported were censored at the time of the mail or telephone follow-up. In a supplementary analysis the definition of success was extended to include all first conceptions except for those arising from IVF or ICSI treatments. Thus, in the supplementary analysis, conceptions resulting from clomiphene citrate or gonadotrophin ovulation induction, artificial insemination by partner and donor insemination treatments were also counted as successes.

Technique and equipment used

The method used has been described elsewhere (Papaioannou et al., 2002a,b). In brief, the Fallopotorque (Cook UK, Letchworth, Hertfordshire, UK) SS/TC catheter system was used. The fluoroscopic unit employed was the mobile Phillips Optimus BV29 with a C-arm system (Phillips Corporation, The Netherlands). The distal end of the SS catheter was connected by polyethylene tubing to a syringe pump (KMAR–400; Cook UK). Water-soluble contrast medium (Hexabrix 320; Mallinckrodt Medical, Round Spinney, UK) at a constant flow rate of 10 ml/min was used.

SS/TC was performed during the follicular phase of the menstrual cycle. The SS catheter was forwarded through the cervical canal and advanced by tactile sensation to the tubal ostium. Its position was checked fluoroscopically and, if satisfactory, dye was injected. If the obstruction was overcome then the tubal contour was outlined with contrast. If it persisted a guidewire was threaded through the inner cannula and advanced by tactile sensation to the tubal ostium. Its position was checked fluoroscopically and, if satisfactory, dye was injected. If the obstruction was overcome then the tubal contour was outlined with contrast. If it persisted a guidewire was threaded through the inner cannula and advanced towards the obstruction. A gentle push was applied to overcome it. The guidewire was then withdrawn and contrast medium was injected through the SS catheter to confirm patency.

Results

From the 218 women included in the study, pregnancy information was collected from 166 (76.1%). Of them, 148 women (89.1%) returned a questionnaire and 18 (10.9%) were interviewed by telephone.

Fallopian tubes

From the 427 available tubes, SS was attempted in 400 tubes and was possible in 367 (91.7%). SS/TC was not attempted in cases where the Fallopian tubes were known either to be normal or to have significant distal disease by a previous HSG or laparoscopy. Acute ante- or retro-version of the uterus, irregular enlargement of the uterine cavity due to fibroids or an acute angle of the Fallopian tube in relation to the uterine cavity were present in the cases where SS was not technically possible.

SS showed PTB in 217 tubes (59.1%), a normal tube in 135 (36.7%), middle tubal block in five cases (1.3%) and
Table I. Pregnancy results by method of conception (only the first conception per subject is considered)

<table>
<thead>
<tr>
<th>Method of conception</th>
<th>No. of conceptions</th>
<th>% Amongst all conceptions</th>
<th>% Amongst women in study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>45</td>
<td>20.6</td>
<td>27.1</td>
</tr>
<tr>
<td>Artificial insemination by partner</td>
<td>5</td>
<td>2.3</td>
<td>3.0</td>
</tr>
<tr>
<td>Clomiphene</td>
<td>1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Ovulation induction</td>
<td>2</td>
<td>0.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Donor insemination</td>
<td>1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>IVF/ICSI</td>
<td>31</td>
<td>14.2</td>
<td>18.7</td>
</tr>
</tbody>
</table>

Not conceived 81 women. Not responded 52 women.

hydrosalpinx in seven (1.9%), while in three cases the reports were judged not to be sufficiently clear for interpretation. Guidewire TC was performed in 215 of the 217 proximally blocked Fallopian tubes. It was technically possible in 196 (91.1%) cases, of which in 99 (50.1%) the tube appeared normal after TC. PTB persisted in 39 cases (19.9%), middle block was identified in five (2.6%), distal block in 13 (6.7%), peritubal adhesions were suspected in 19 (9.7%) and a hydrosalpinx was revealed in 18 (9.2%) cases. In three cases (1.6%) there was uncertainty about the interpretation of the SS/TC reports.

Patients
From the 76 women who were referred for SS/TC because of bilateral PTB, after SS, bilateral PTB persisted in 41 (53.9%), while unilateral PTB was present in 21 (27.6%). Following tubal catheterization, bilateral PTB was present in eight (10.5%) and unilateral PTB in six (7.8%) women.

From the 78 patients who were referred for SS/TC because of unilateral PTB, after SS, 16 (20.5%) were classified as having bilateral PTB, while unilateral PTB persisted in 28 (35.8%) women. Following TC, there were no women with bilateral PTB, while unilateral PTB was present in eight cases (10.2%).

Pregnancy results
The number of pregnancies by method of conception, when only the first conception for each woman was considered, is shown in Table I.

Two groups were studied: women ≤35 years of age (n = 109, spontaneous conceptions 36, other non-IVF/ICSI conceptions eight) and women ≥36 years of age (n = 56, spontaneous conceptions nine, other non-IVF/ICSI conception one). Figure 1 shows the cumulative conception rates for spontaneous first conceptions for the two age groups as well as the conception hazard rate for women ≤35 years of age. Figure 2 shows the cumulative conception rates for all non-IVF/ICSI conceptions. Conception rates were significantly higher in the younger age group (P = 0.023 spontaneous conceptions and P = 0.007 for non-IVF/ICSI conceptions, log-rank test). There were 36/148 (24.3%) spontaneous conceptions amongst the mail responders and 9/18 (50%) amongst the telephone responders (P = 0.045, two-tailed Fisher’s exact test).

During the study period, in total there were 66 spontaneous conceptions (see below), five conceptions after artificial insemination by partner, two after ovulation induction with gonadotrophins, one after clomiphene citrate treatment and one after donor insemination treatment. Of these 43 (57.3%)
resulted in live births, five (6.7%) were ongoing at the time of the survey (all >20 weeks gestation), 19 (25.3%) resulted in miscarriages and eight (10.7%) in ectopic pregnancies.

A number of women conceived more than once during the study period. In nine cases there were two and in two cases there were three spontaneous conceptions. Two women conceived spontaneously after having conceived with artificial insemination for the first time, one after having conceived with ovulation induction and another after having conceived on clomiphene citrate the first time. Four women conceived spontaneously after becoming pregnant with either IVF or ICSI treatments the first time. Therefore, spontaneous conceptions reported during the study period after these women had conceived once following the procedure were 5 + 4 + 2 + 1 + 1 + 4 = 21, plus 45 spontaneous first conceptions, giving a total of 66.

No significant difference was identified in the number of non-IVF/ICSI conceptions reported by women according to whether the diagnosis of PTB was reached by HSG ($n = 105$, results available for 81, conceptions = 30), by laparoscopy and dye test ($n = 50$, results available for 38, conceptions = 8) or by both tests ($n = 63$, results available for 47, conceptions = 16). This did not change when only spontaneous conceptions were considered ($P = 0.21$ and $P = 0.36$ respectively, $\chi^2$-test).

When non-IVF/ICSI conceptions were analysed according to whether bilateral PTB ($n = 76$, results available for 58, conceptions = 21) or unilateral PTB ($n = 78$, results available for 68, conceptions = 23) was present, again no significant difference was identified. The same was the case when only spontaneous conceptions were considered ($P = 0.92$ and $P = 0.56$ respectively, $\chi^2$-test).

Women with previous sterilization reversal or tubal surgery

In the group of five women that had SS/TC after sterilization reversal surgery, nine Fallopian tubes were available. No tubes were successfully recanalized, despite guidewire tubal catheterization being attempted in all cases. Surprisingly, one of the four women in this group from whom responses were collected conceived spontaneously ~7 months after the procedure. Unfortunately the pregnancy resulted in a first trimester miscarriage. Two others conceived with IVF treatment.

There were 11 Fallopian tubes available in the group of six women that had undergone tubal surgery before SS/TC. SS was performed in nine tubes, of which two were found to be normal and seven (77.7%) to be proximally blocked. Of them, two were successfully recanalized. Distal tubal disease was present in both cases. There were no spontaneous conceptions reported by the four women in this group from whom responses were collected (two conceived with IVF treatment).

Complications

Perforation of a Fallopian tube occurred in five cases (2.3%). No treatment was necessary for any of these women. Two patients (0.9%) experienced a vasovagal reaction, which was treated successfully with the administration of i.v. fluids. One woman (0.4%) had to be admitted to the hospital after SS/TC because of pain. She was discharged the same day. Intravasation of contrast agent was noted in nine cases (4.1%).

Discussion

This study presents the results of a survival analysis of conception rates following SS/TC in a group of 218 infertile women with PTB. Follow-up ranged from 16 to 57 months. It shows that, even in the presence of additional infertility factors, a significant proportion of spontaneous (as well as other non-IVF/ICSI) conceptions in this population occur after the first 12 months following the procedure (47.2 and 43.2% respectively in our study). Inspection of the smooth (Weibull) conception hazard rate in Figure 1 shows that this decreases only slightly over the period following SS/TC.

This finding contradicts the result of previous studies of SS/TC, which found that the possibility of spontaneous fertility diminishes once the first few months after SS/TC have elapsed (Lang et al., 1990; Thurmond and Rosch, 1990; Darcy et al., 1991). The relatively short follow-up periods in these studies limit the generalizability of their conclusions. In most other series of SS/TC, only cumulative conception rates are reported, without any reference to rates at different intervals within the study follow-up period (Kumpe et al., 1990; Capitano et al., 1991; Thurmond, 1991; Woolcott et al., 1995).

The only previous survival analysis presentation of conception rates after SS (TC was not performed) in the literature included 16 women with PTB, enrolled in the multicentre transcervical balloon tuboplasty study (Gleich et al., 1993). Pregnancies were still being recorded at 2 years following the procedure.

Our study presents for the first time conception rates following SS/TC in a series of consecutive infertile women with PTB. No exclusion criteria were applied. Such results are closer to everyday clinical practice than reports on pregnancy rates following SS/TC in ideal, carefully selected samples of infertile women without any additional infertility factors. Our results should be generalizable in settings similar to ours. Information about conceptions achieved with the aid of fertility treatments (excluding IVF and ICSI), is provided to illustrate the total therapeutic impact of SS/TC in this population. Once Fallopian tube patency is re-established, ovulation induction, artificial insemination by partner and donor insemination become feasible treatment options, a fact also demonstrated by previous authors (Motta et al., 1995). These treatments are safer and far less expensive than IVF that would be, in the absence of SS/TC, the only alternative for women when the Fallopian tubes are found to be proximally blocked.

With emphasis placed on the therapeutic results of SS/TC, its diagnostic benefits are often overlooked. In our population, middle tubal block or distal tubal disease was revealed after tubal catheterization in 55 of 215 (25.5%) of Fallopian tubes found to be proximally blocked at SS. In such cases, the background spontaneous conception rate might not be significantly improved (although still patent Fallopian tubes should be better than blocked tubes). However, a laparoscopy, which would usually follow an abnormal HSG, can be avoided.
On the other hand, in cases of unsuccessful SS/TC there is almost always, sometimes multiple, organic tubal pathology (Letterie and Sakas, 1991; Hilgers and Yeung, 1999) and again, if IVF treatment is possible, laparoscopic evaluation becomes unnecessary. In terms of diagnostic accuracy, SS/TC is equally good, if not superior to diagnostic laparoscopy (Woolcott et al., 1999) given the fact that in most cases of organic proximal blockage, no indication of abnormality can be identified at laparoscopy (Hilgers and Yeung, 1999). The salpingographic demonstration of ‘cobblestone’ mucosa in the distal Fallopian tube has been associated with irreversible mucosal damage (Lang and Dunaway, 2001).

Interestingly, four women conceived spontaneously after previously, during the study period, becoming pregnant with either IVF or ICSI treatments following SS/TC. Another four women conceived spontaneously after initially becoming pregnant with the aid of other fertility treatments after SS/TC, used because of the co-existence of other infertility factors in these couples. One woman with previous sterilization reversal surgery conceived spontaneously after SS/TC was unsuccessful in recanalizing the Fallopian tubes. Spontaneous conceptions after unsuccessful attempts at SS/TC have also been previously reported in the literature (Ferraiolo et al., 1995). A spontaneous intrauterine conception has even been achieved after SS/TC complicated by tubal perforation (Capitianio et al., 1991). Based on this background, it would be plausible to assume that even in cases in which SS/TC is judged to be unsuccessful either on the basis of its immediate results, or because of the lack of conception during an initial follow-up period, the procedure still does have a positive impact on pregnancy rates.

There was a 2.3% cancellation rate in our series. No reference to women who did not undergo SS/TC despite that being the initial intention is made in previous studies. In two out of five such cases in our series, the reason for cancellation was essentially the patient’s anxiety about the procedure. Perhaps more information about the procedure and explanation of its steps as well as direct questioning about the woman’s previous experiences of gynaecological examinations could have prevented this. The fact that, in contrast with other groups, sedation is not used for our patients may be a contributing factor. Nevertheless, we believe that this percentage is within acceptable limits, and not a sufficient reason to introduce a policy of routine sedation for women undergoing SS/TC with its associated side-effects and costs.

The results of SS/TC in women with previous sterilization reversal or tubal surgery in our population were disappointing. Only two out of 16 tubes (12.5%) were successfully recanalized with distal tubal disease present in both cases. Out of 11 women in this group, we are aware of one spontaneous conception (9%). More favourable results after SS/TC in such patients have been reported by other groups with recanalization rates ranging from 52 to 68% and intrauterine pregnancy rates from 15 to 30% (Lang and Dunaway, 1994; Thurmond et al., 1999). A high incidence of distal tubal disease in such cases has been reported previously (Lang and Dunaway, 1996). The presence of intravasation of the contrast agent or of a fistula at the anastomotic site has been associated with failure of recanalization in all cases (Lang, 1995, 1998). The cause of tubal obstruction in the post-operative Fallopian tube is not always scar tissue formation and therefore SS/TC can be attempted. However, depending on the specifics of the individual case (age, operative findings, additional infertility factors etc.), even in ideal cases of successful SS/TC, an earlier resort to alternatives is indicated. In this group of patients, >6 months of follow-up without offering alternatives may waste valuable time (Thurmond et al., 1999).

Considerable pessimism has been expressed in the past about the possibility of an intrauterine conception for women after guidewire tubal cannulation was used (Gleicher et al., 1994; Woolcott et al., 1995). Our data did not confirm this view. When pregnancies were analysed according to whether women had undergone bilateral, unilateral or no guidewire tubal catheterization, no significant differences were identified (Afnan et al., 2001).

Only a small minority of the pregnancies recorded during the study period were the result of ovulation induction treatment. These data further indicate that ovulation induction is not the treatment of choice in cases where there is any indication of tubal disease.

A possible source of bias in the study design used would be a higher response rate amongst women who conceived after SS/TC and therefore a relative under-representation of the group of responders who did not. In the current study, the proportion of spontaneous conceptions amongst women who did not respond to the letters and were later interviewed by telephone was, to our surprise, significantly higher than that of women who returned a questionnaire. This means that the motivation for mail responders to send their questionnaires back was not necessarily their gratitude for a successful outcome and vice versa. Therefore, our results should not be biased by the representation of women who did not conceive. The response rate (76.1%) was well over the accepted standard of 70%, a percentage above which most biases become minimal (Lydeard, 1996).

Another possible source of criticism of our study might be the fact that in a significant proportion of our population, the diagnosis of PTB was made on a single HSG. In other studies of SS/TC, women with PTB were selected after multiple tubal assessment tests had confirmed the diagnosis. This means that some women with a false positive initial diagnosis of PTB might have been included in the present study. Given the fact that Fallopian tubes that are consistently demonstrated to be proximally blocked on multiple tests can still be found to be patent later (Gleicher et al., 1993), this is a possibility in all study models. Furthermore, this study aims to describe the use of SS/TC in everyday clinical practise rather than under research conditions. Therefore, it is questionable whether multiple tests (including a diagnostic laparoscopy) would be justified in this context, especially given the safety record of SS/TC, both in the short and in the long term (Papaioannou et al., 2002b).

It may be argued that pregnancies that occur after treatment of bilateral PTB should be reported separately from pregnancies that occur after treatment of unilateral PTB, as these conceptions cannot necessarily be attributed to the recanalized fallopian tubes...
Fallopian tube. Although nobody can disagree with this fact, treatment of unilateral PTB with SS/TC is recommended as it signiﬁcantly improves the intrauterine pregnancy rate (Hovsepian et al., 1994). Furthermore, this study aimed to explore the place of SS/TC in an unrestricted infertile population with PTB, and therefore the adoption of such a policy would exclude a significant number of subjects.

There were a significant number of cases where it was not possible to identify information about the results of other infertility investigations, or even the presence of unilateral or bilateral PTB before SS/TC. This was mainly due to the fact that a signiﬁcant number of women referred from other hospitals speciﬁcally for SS/TC were described only as having been diagnosed with PTB, without much further information provided.

In conclusion, the results presented here suggest that the necessity of IVF treatment in infertile women who do not conceive during an initial observation period following SS/TC is relative and not absolute. Space for individual management of the individual case exists. In addition, the presence of any infertility factors in addition to PTB in a couple should not necessarily be a contraindication to SS/TC. Even in cases where SS/TC is judged to be unsuccessful, diagnostic and even therapeutic beneﬁts might still be gained. SS/TC provides the opportunity for reliable tubal assessment combined with safe, minimally invasive treatment. The above would justify the more widespread use of SS/TC in the management of the infertile couple.

References


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