Diagnostic tests for tubal pathology from a clinical and economic perspective

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History of induced abortion and the risk of tubal pathology

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Abstract

Background

Tubal pathology is a common cause for subfertility. Identifying risk factors in the medical history for tubal pathology is important to distinguish between those couples who benefit from early tubal patency tests and those in whom presence of tubal pathology is less likely and delaying tubal tests is justified. Induced abortion mostly implies an unplanned or unwanted pregnancy and is associated with an increased risk of genital tract infections. We therefore hypothesized that a history of induced abortion is associated with an increased risk of tubal disease in subfertile couples.

Methods

We performed a retrospective hospital based cohort study. For each couple, the reproductive history was registered. Tubal disease was diagnosed by hysterosalpingography and/or diagnostic laparoscopy. We assessed the association between reproductive history and the presence of tubal disease, by calculating odds-ratios (OR) and 95% confidence intervals.

Results

Data from 6,149 couples were available for analysis. The OR for tubal pathology after a previous induced abortion was 1.6 (95% CI: 1.3 to 1.9), after a previous ectopic pregnancy 8.4 (95% CI: 6.3 to 12), after a previous miscarriage 1.1 (95% CI: 0.87 to 1.3), and after a previous live birth 1.0 (95% CI: 0.88 to 1.2).

Conclusions

A history of induced abortion is associated with an increased risk of tubal pathology in subfertile couples. As a consequence, in subfertile women with a history of induced abortion, tubal patency tests should be considered early in the diagnostic work-up.

Introduction

The aim of the fertility work-up is to detect or exclude recognized causes of infertility and to distinguish those couples who have good spontaneous pregnancy prospects from those who have poor prospects. The work-up for subfertility starts with taking a thorough medical history of the couple. In current practice, hysterosalpingography and laparoscopy combined with chromopertubation are the two methods mostly used to assess tubal patency in subfertile women. Both tests are invasive and a burden to the patient, moreover, laparoscopy is expensive. For these reasons tubal patency tests are usually performed at the end of the fertility work-up. Tubal pathology is responsible for about 14% of the causes for subfertility (Hull *et al*.,1985). The prevalence depends on whether one deals with a primary-care, secondary-care or tertiary-care population (Evers, 2002).
Identifying risk factors for tubal pathology in the medical history is important since this might affect the strategy for tubal patency testing, by planning these tests earlier in the work-up. If bilateral tubal occlusion is present and surgical correction is not feasible, patients should be offered in-vitro-fertilization (IVF), because their chances of a spontaneous pregnancy or after intra uterine insemination are almost nihil (Mol *et al*.,1999). Known risk factors for tubal subfertility are a previous diagnosis of PID or salpingitis (Westrom *et al*., 1975, Paavonen *et al*., 1999), a previous salpingitis as shown by a positive *Chlamydia* Antibody Titer (CAT) (Thomas *et al*., 2000), abdominal surgery (Trimbos-Kemper *et al*., 1982) or severe endometriosis (Crosignani *et al*., 2006). Induced abortion mostly implies an unplanned or unwanted pregnancy and is associated with an increased risk of genital tract infections (RCOG guideline, 2004). We therefore hypothesized that a history of induced abortion is associated with an increased risk of tubal disease in subfertile couples.

Materials and methods

In this retrospective cohort study, data from 1984 onwards, of all patients presenting at the Onze Lieve Vrouwe Gasthuis (Amsterdam) with subfertility, were entered prospectively in an electronic database. The department of reproductive medicine is situated in an inner city teaching hospital. For each couple we registered the reproductive history, i.e. previous life births, induced abortions, ectopic pregnancies, and miscarriages. We also recorded female age and the presence of male subfertility or cervical factor subfertility. From all male patients two semen samples were analysed. Male subfertility was defined according to World Health Organisation criteria: semen with a volume < 2.0 mL, pH < 7.2, concentration<20 million/mL, < 50% progressive motile spermatozoa within 1 hour of ejaculation, < 15% normal morphology of the semen (World Health Organisation,1999). The menstrual cycle was evaluated by a basal body temperature chart or luteal phase progesterone value. All patients underwent a post-coital test pre-ovulatory. Correct timing was evaluated by assessing the quality of the cervical mucus and

by ultrasound imaging of the ovaries. Cervical factor subfertility was classified as an abnormal post-coital test in the presence of normal semen parameters. Presence of tubal disease was assessed by hysterosalpingography (HSG) and/or diagnostic laparoscopy and defined as tubal occlusion of at least one tube or presence of abnormalities believed to be responsible for the subfertility. All women underwent a HSG. If the HSG was abnormal, a laparoscopy followed to either confirm or refute the findings at HSG. Presence of tubal pathology was decided upon the laparoscopic findings. To assess the association between induced abortion and the presence of tubal disease, we cross tabulated reproductive history and presence of tubal pathology. Subsequently we calculated Odds Ratios (OR) and their 95% confidence intervals. To assess whether the result of the univariable analysis was affected by confounding, we also performed a multivariable analysis, in which we controlled for age, as well as male subfertility or cervical factor subfertility.

Results

In the study period from 1984 to 2001, data from 6,149 couples were registered. There were 2,944 couples with primary subfertility and 3,205 couples with secondary subfertility. The median female age was 33.5 years (21-44 years). Tubal pathology was diagnosed in 19.8% of the couples. Of the 3,205 women with a previous pregnancy, 278 had at least two types of pregnancy i.e. for example live-birth and previous miscarriage, or other combinations. Tubal pathology was present in 207 (25%) of 826 women with a previous induced abortion, in 145 (64%) of 226 women with a previous ectopic pregnancy, in 139 (19%) of 748 women with a previous miscarriage and in 301 (19%) of 1683 women with previous live-births. Tubal pathology was present in 94 women (6.4%) where male subfertility (1474 or 24%) was diagnosed and in 14 women (6%) where cervical factor subfertility (227 or 3.7%) was diagnosed. In the univariable analysis, previous induced abortion was associated with a mildly increased risk of tubal pathology (OR 1.6, 95% CI 1.3 to 1.9), whereas for previous ectopic pregnancy this was strongly increased (OR 8.4, 95% CI 6.3 to 12). Previous miscarriage and previous live-birth were not related to tubal pathology, OR 1.1 (95% CI 0.87 to 1.3) respectively 1.0 (95% CI 0.88 to 1.2). Of the other variables, increasing female age per year increased the probability of tubal pathology (OR 1.05, 95% CI 1.04 to 1.06), whereas presence of male subfertility or cervical factor subfertility decreased the probability of tubal pathology OR 0.25 (95% CI 0.20 to 0.31) respectively 0.29 (95% CI 0.17 to 0.50). Multivariable logistic regression did not change the results of the analysis.

Discussion

In this large cohort study we demonstrated that women with secondary infertility and a history of induced abortion have a statistically significant increased risk of tubal pathology. We know

of four previous studies that assessed the relationship between a history of induced abortion and tubal pathology as diagnosed either by HSG and/or laparoscopy or laparotomy, which all had a case-control design (Daling *et al*., 1985, Lalos, 1988, Minh *et al*., 2002, Torres-Sanchez *et al*., 2004), (Table 1). These studies did not show a significant association between a history of induced abortion and tubal pathology. However, the results of these studies are possibly flawed by their design. First, they were underpowered to detect a small effect of induced abortion on secondary tubal infertility. Our study is the largest cohort study to date, consisting of 6,149 couples, which increases the statistical power to assess whether an association between a history of induced abortion and tubal pathology truly exists. Second, case-control studies of this kind are sensitive to selection bias. Cases and controls could have had too unequal chances of being exposed to induced abortion for them to be comparable. Because we used a cohort design, this bias could not influence the analysis in our study. Third, the socio-economic background of both cases and controls in these studies could have been different, leading to differences in uptake of medical care between the subfertile patients and the pregnant controls. A fertility work-up is expensive, but is in the Netherlands covered by compulsory health insurances. The results of our study are therefore not confounded by the fact that only patients who can afford expensive fertility examinations seek medical care, or that our population mainly exists of women with a higher socio-economic status, as in the other studies (Daling *et al*, 1995,Torres-Sanchez *et al*., 2004). A limitation of our study is that not all women underwent a laparoscopy. If HSG did not show any abnormalities a laparoscopy was not performed. HSG gives a morphological view of the uterine cavity, the fallopian tubes and their patency with a sensitivity of 65% and a specificity of 83% compared to laparoscopy (Swart *el al*.,1995). This could have led to an underestimation of the presence of tubal pathology since HSG does not allow to assess the presence of pelvic adhesions, either caused by infections or endometriosis, as in contrast to laparoscopy.

In our population tubal pathology accounted for almost 20% of the diagnosis of subfertility. In the Netherlands induced abortion is legalised since 1984 and the procedure is generally performed under safe conditions and reimbursed. The majority of these procedures are instrumental first trimester abortions and are performed in specialised clinics or hospitals (Jaarrapportage, 2004), this in contrast to countries where induced abortion is not allowed by legislation and illegal abortion can lead to significant morbidity, including infertility and even mortality of the woman (Kadayifci *et al*. 2007).

What do our findings mean? It is well known that a history of PID – the single most important risk factor for tubal pathology- is associated with induced abortion (Shrikhande *et al*., 1998, Daling *et al*.,1985, Torres-Sanchez *et al*.,2004) and since induced abortion in the Netherlands is performed with the same care and under similar sterile conditions as evacuation of a miscarriage, in which we did not find an increased risk of tubal pathology, our findings are in support of PID being the cause of tubal pathology and not the procedure of evacuating the uterine cavity of the products of conception. The same argument can be made for the risk factors early

Table 1

Published articles addressing relation of tubal infertility with induced abortion

Authors	Publication	Type of study	Size of study	Outcome OR (95% CI)
Daling *et al*.	Fertil Steril. 1985	Population based Case-control	127 with known diagnosis of tubal infertility 395 women who conceived a child at same time as infertile women began attempt to become pregnant	1.15 (0.70 to 1.9)
Lalos	Eur J Obstet Gynecol Reprod Biol. 1988	Hospital based Case-control	120 with known diagnosis of tubal infertility 126 pregnant women	0.49 (0.25 to 0.96)
Minh *et al*.	Fukushima J Med Sci. 2002	Hospital based Case-control	67 women with diagnosis of tubal infertility 67 women who underwent caesarian section with intact tubes confirmed at operation	1.27 (0.64 to 2.5)
Torres-Sanchez *et al*.	BJOG 2004	Population- and hospital based Case-control	251 with known diagnosis of tubal infertility 1004 women with a history of pregnancy during two preceding years or pregnant at the time date of interview	0.82 (0.07 to 9.0)* 1.6 (0.29 to 8.7)π

* cases vs neighbourhood controls
π cases vs hospital controls

sexual activity, unsafe sex, high prevalence of *C. Trachomatis* and a high number of sexual partners which all increase the risk for PID (Jossens *et al*., 1996, Simms *et al*., 2006).
Unfortunately, we could not control for sexual behaviour and a history of PID or presence of *Chlamydia* antibodies, since we introduced this test in our clinic from 1999 onwards. Although our data do not indicate that induced abortion is the cause of the tubal pathology, but a risk marker for other factors that cause tubal subfertility, the clinical importance of our study is that the risk of tubal disease in women presenting with subfertility is increased once they report a history of induced abortion. This is especially important, since tubal subfertility can be the result of asymptomatic or silent PID, which for this reason will not be revealed and recorded in the medical history. This means that invasive diagnostic tests such as laparoscopy should be considered at an earlier stage of the fertility work-up. On the other hand, we found that in couples where cervical factor subfertility or male subfertility is present, the risk of tubal pathology is decreased, thus justifying a postponement of invasive tests for tubal disease.

Conclusion

Women with a history of induced abortion have an increased risk of tubal subfertility. Diagnostic tests for tubal patency earlier in the fertility work-up, should be considered.

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