

Prevalence of Asherman's syndrome after secondary removal of placental remnants or a repeat curettage for incomplete abortion

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This prospective study assesses the prevalence of intrauterine adhesions among women undergoing secondary removal of placental remnants after delivery, or a repeat curettage for incomplete abortions, and evaluates risk factors associated with the presence of intrauterine adhesions. In 50 women, undergoing either a secondary removal of placental remnants more than 24 h after delivery, or a repeat curettage for incomplete abortions, ambulatory hysteroscopy was performed 3 months after the intervention. Intrauterine adhesions were found in 20 of the women (40%): five patients had Asherman's syndrome grade I, six had grade II, six had grade III and three had grade IV. In women with menstrual disorders a statistically significant 12-fold increased risk for Asherman's syndrome grade II–IV was found. Previous abortion as well as infection during surgery were associated with a mildly but non-significant increased risk. Based on our findings, hysteroscopy is recommended only in those patients who develop menstrual disorders, either after secondary intervention for placental remnants after delivery or after a repeat curettage.

Key words: Asherman's syndrome/curettage/hysteroscopy/intrauterine adhesions/menstrual disorders

Introduction

In 1948 Joseph G. Asherman described the syndrome of intrauterine adhesions, which has borne his name ever since (Asherman, 1948, 1950). In his original description, Asherman differentiated between 'traumatic intrauterine adhesions' which did not necessarily result in menstrual disturbances, and 'atretic amenorrhoea', where amenorrhoea was present as a result of cervical adhesions. Difficulties in establishing the diagnosis of Asherman's syndrome were solved with the introduction of hysteroscopy. This method supplied the reference standard for diagnosing and classifying intrauterine adhesions, and provided the elementary tools for treatment.

Intrauterine adhesions can cause menstrual disturbances, infertility, recurrent abortions and, when pregnancy occurs,

premature labour, placenta previa or placenta accreta (Schenker and Margalioth, 1982). Intrauterine adhesions may be present not only when amenorrhoea or hypomenorrhoea occurs, but also in eumenorrhoeic women (Taylor *et al.*, 1981). Early detection is of importance, since hysteroscopic treatment is often possible and can prevent further complications (Valle and Sciarra, 1988; Goldenberg *et al.*, 1995).

As aetiological determinants of Asherman's syndrome, trauma to the uterine cavity by curettage (especially of the puerperal uterus), local infection, or a combination of these factors, are generally accepted causes (Schenker and Margalioth, 1982). Very little, however, is known about the incidence of Asherman's syndrome in women exposed to these events. Thus far, few prospective studies using hysteroscopic criteria assessed the incidence after a curettage for missed abortion (Lurie *et al.*, 1991; Golan *et al.*, 1992; Friedler *et al.*, 1993; Römer, 1994). Asherman's syndrome was reported to be present in almost 20% of the patients, the majority being of mild extent and of filmy consistency. Data on prevalence of intrauterine adhesions after secondary puerperal procedures are scarce (Jensen and Stromme, 1972; Golan *et al.*, 1996).

The present study assesses the prevalence of intrauterine adhesions in women assumed to be at increased risk for developing intrauterine adhesions: women undergoing secondary procedures for placental remnants after delivery, or a repeat curettage after a previous incomplete curettage for missed or medical abortion.

Materials and methods

From May 1989 to January 1995, two groups of patients were recruited in the Academic Medical Centre in Amsterdam, The Netherlands. All patients undergoing digital evacuation and/or curettage for placental remnants more than 24 h after delivery and patients undergoing a repeat curettage for retained products of conception after a previous incomplete curettage for missed or medical abortions were entered in a prospective study. During these procedures antibiotics were administered as a single prophylactic dose in patients without fever, or therapeutically as a 7 day course in those with fever (temperature $\geq 38^{\circ}\text{C}$). Three months after this intervention, all women were examined hysteroscopically to assess the presence of intrauterine adhesions. The study was restricted to patients who were primarily treated in our department; patients referred from other units for suspected Asherman's syndrome were not included. Approval for the study was obtained from the appropriate local committees on ethical practice and informed consent was obtained from all participants.

Data concerning the presence of menstrual disturbances, use of contraceptive methods and the practice of breastfeeding were collected from the medical files by a research assistant.

Hysteroscopy was conducted on an outpatient basis with local anaesthesia, using rigid 7 mm Storz equipment (Karl Storz GmbH &

Table I. Risk of Asherman's syndrome grade II–IV

| Risk factor | Grade 0 | Grade I | Grade II–IV | RR | 95% CI | <i>P</i> |
|-------------------------|---------|---------|-------------|------|----------|----------|
| Previous abortions | 8 | 2 | 6 | 1.4 | 0.61–3.3 | 0.64 |
| Infection (fever >38°C) | 9 | 3 | 6 | 1.2 | 0.50–2.8 | 0.66 |
| Hormonal influences | | | | | | |
| None | 18 | 2 | 8 | 1.0 | – | – |
| Lactation | 1 | 0 | 3 | 2.6 | 1.2–5.9 | 0.04 |
| OC or MPA | 12 | 4 | 3 | 0.55 | 0.17–1.8 | 0.31 |
| Unknown | 0 | 0 | 1 | – | – | – |
| Menstrual cycle | | | | | | |
| Normal | 21 | 1 | 1 | 1.0 | – | – |
| Amenorrhoea | 2 | 2 | 8 | 15 | 2.1–109 | <0.0001 |
| Hypomenorrhoea | 6 | 1 | 3 | 6.9 | 0.81–59 | 0.13 |
| Dysmenorrhoea | 0 | 1 | 2 | 15 | 1.9–122 | <0.0001 |
| Any disorder | 8 | 4 | 13 | 12 | 1.7–58 | <0.0001 |
| Unknown | 1 | 0 | 1 | – | – | – |

RR = relative risk; CI = confidence interval; OC = oral contraceptives; MPA = medroxyprogesterone acetate.

Co., Tuttlingen, Germany). The hysteroscope was inserted into the uterine cavity under direct video control. To prevent any unnoticed perforation of cervical adhesions, blind dilation of the cervix by probes was withheld whenever possible. For distension of the uterine cavity 32% Dextran 70/10% dextrose was used (Hyskon®; Kabi Pharmacia Inc., Clayton, USA). The severity and extent of intrauterine adhesions was expressed in grades 0–IV, based on the classification of the European Society of Hysteroscopy (Wamsteker, 1990).

The association between various clinical parameters and the presence of intrauterine adhesions grade II–IV was analysed by calculating a relative risk (RR), 95% confidence intervals (CI) and *P* values, using SPSS 7.5 for Windows (Altman, 1991). Clinical parameters were: fever during the primary intervention, previous abortion and menstrual pattern. The relationship between oestrogenic state and the occurrence of adhesions was assessed by comparing risk of lactating women (low oestrogenic state) and women using combined oral contraceptives or medroxyprogesterone acetate (high oestrogenic state) to that of women without specific hormonal influences, who were assumed to have intermediate oestrogen concentrations.

Results

Fifty women, aged 19–44 years (mean 31.8 years) were entered in the study. A secondary puerperal procedure for placental remnants was the reason for entrance in 40 cases (puerperal group), a repeat curettage after a previous incomplete curettage for missed or medical abortion in 10 cases (abortion group). The mean gestational age was 29.6 weeks (SD 10.3) in the puerperal group and 12.3 weeks (SD 2.8) in the abortion group. Intrauterine adhesions were encountered in 20 out of 50 patients (40%); five patients had grade I, six had grade II, six had grade III and three had grade IV. The risk for Asherman's syndrome grade II–IV was 30% both in the puerperal group (12/40) and in the abortion group (3/10).

Table I relates several possible risk factors for development of intrauterine adhesions to the hysteroscopic findings. Among 16 women with a previous abortion, six developed Asherman's syndrome grade II–IV (RR 1.4, 95% CI 0.61–3.3, *P* = 0.64). Among 18 patients with clinical signs of infection during surgery, six developed Asherman's syndrome grade II–IV (RR 1.2, 95% CI 0.50–2.8, *P* = 0.66).

Among 17 women using oral contraceptives or medroxyprogesterone acetate, three developed Asherman's syndrome grade II–IV (RR 0.55, 95% CI 0.17–1.8, *P* = 0.31). Only four women reported lactation, and three of them turned out to have Asherman's syndrome grade II–IV (RR 2.6, 95% CI 1.2–5.9, *P* = 0.04). Among the 17 women using oral contraceptives or medroxyprogesterone acetate, 10 had no menstrual disorders, two had amenorrhoea, two had hypomenorrhoea and three had dysmenorrhoea. All four women reporting lactation also had amenorrhoea.

Among 23 women with normal periods, severe adhesions were present in only one. In contrast, in 12 women with amenorrhoea, severe Asherman's syndrome was present in eight (RR 15, 95% CI 2.1–109, *P* < 0.0001); in 10 women with hypomenorrhoea, severe Asherman's syndrome was present in three (RR 6.9, 95% CI 0.81–59, *P* = 0.13); whereas in three women with dysmenorrhoea Asherman's syndrome was present in two (RR 15, 95% CI 1.9–122, *P* < 0.0001). Overall, among 25 with any menstrual disorder, 13 had severe Asherman's syndrome (RR 12, 95% CI 1.7–58, *P* < 0.0001).

Discussion

In this prospective study among women undergoing secondary interventions for placental remnants after delivery and women undergoing a repeat curettage after curettage for missed or medical abortion, Asherman's syndrome was found in 40% of women, of whom 75% had grade II–IV. Women with menstrual disorders after the intervention had a strongly increased risk for developing intrauterine adhesions. A previous abortion as well as infection during surgery generated a slightly increased risk that was not statistically significant.

Due to its prospective design, our study provides a good opportunity to study the prevalence of intrauterine adhesions in a group of presumed high-risk patients. To exclude selection bias, patients referred to our hospital from other units for suspected Asherman's syndrome were not included in the study. Strict adherence was paid to the classification system of the European Society of Hysteroscopy. Since we could not assess the presence of intrauterine adhesions in women before

entering the study we cannot evaluate whether pre-existing adhesions, possibly resulting from previous intrauterine procedures, confounded the estimation of the prevalence of intrauterine adhesions. In our study group, however, we did not find an association between the number of reported previous intrauterine procedures and the presence of intrauterine adhesions, and adjustment for the number of previous intrauterine procedures did not change our estimates.

Adoni *et al.* (1982), using hysterosalpingography, found intrauterine adhesions in 15% of 120 patients 6–8 weeks after missed and early abortion. Friedler *et al.* (1993), using hysteroscopy, found an incidence of 19% of intrauterine adhesions after missed abortion. Golan *et al.* (1992) found an incidence of 17% after missed abortion. Römer (1994) found an incidence 30% of women after dilatation and curettage for incomplete or missed abortions. Lurie *et al.* (1991) found a prevalence of 39% among women who underwent curettage after induced midtrimester abortions. We studied the presence of intrauterine adhesions in women undergoing a second curettage after curettage for missed or medical abortion, and found an even higher prevalence of 50%. The prevalence of intrauterine adhesions after manual removal of the placenta were shown to be 2% (Golan *et al.*, 1996), but higher (37.5%) after secondary procedures after postpartum curettage in the second, third or fourth week after delivery (Eriksen and Kaestel, 1960; Jensen and Stromme, 1972). In our study, assessing prevalence after secondary procedures more than 24 h after delivery, we found similar results.

The presence of fever during the intervention raised the relative risk for development of intrauterine adhesions, although not statistically significant. Antibiotics, administered therapeutically in febrile patients, might have diminished the possible stronger development of adhesions in these patients, thereby attenuating a true association.

In our study, despite the small number of lactating women, lactation was shown to carry a significantly increased risk of developing intrauterine adhesions. Assuming lactation to be a proxy for hypo-oestrogenism, this finding supports the theory that low oestrogenic state does influence development of intrauterine adhesions. The number of lactating women in our study was very small, however, and conclusions from this finding should be drawn with caution.

The use of oral contraceptives was associated with RR 0.55 for developing intrauterine adhesions, but this finding was not statistically significant (95% CI 0.2–1.8). Possibly more patients are needed to demonstrate a protective effect, but on the other hand, although it is generally believed, no study has shown the evidence to definitively prove oestrogen supplementation prevents the development of intrauterine adhesions (Friedler *et al.*, 1993; March *et al.*, 1995). A problem in the interpretation of these findings is that patients using contraceptives were less likely to have menstrual disorders, which were also found to be a strong risk factor. Thus, the observed decreased risk for Asherman's syndrome in women using contraceptives might partly be a result of the fact that these women had a normal menstrual pattern before they started contraceptives. Due to the low number of subjects in this analysis, we could not answer this question in this study (Diamond, 1989).

The clinical significance of filmy adhesions — in 10% of our cases — is presently unknown. They might play a role in infertility, but it is likely that these are of minor importance. Grade I adhesions can usually be swept away easily during diagnostic hysteroscopy (Taylor *et al.*, 1981). The high prevalence (30%) of grade II–IV adhesions among our patients is of more concern. Because these adhesions are associated with infertility, menstrual disturbances, and placenta accreta whenever pregnancy does occur, treatment is usually indicated (Valle *et al.*, 1988; Goldenberg *et al.*, 1995). This, however, may not be easy. A sophisticated surgical approach is demanded to find the right cleavage plane in the obliterated uterine cavity. This type of hysteroscopic surgery can, in general, best be performed under laparoscopic guidance to prevent perforation, while simultaneous X-ray fluoroscopy may be required to identify the tubal ostia. Also, transcervical resectoscopy combined with prior insertion of laminaria tents has been shown recently to be a safe and effective means to restore the uterine cavity in case of severe intrauterine adhesions (Chen, 1997).

Retained products of conception clearly represent a serious clinical problem, and prevention is essential. Prompt intervention, i.e. manual exploration of the uterus and removal of any retained cotyledons, is mandatory whenever the situation is suspected. The present study has shown that a normal menstrual cycle virtually rules out the presence of Asherman's syndrome grade II–IV. Consequently, we advise hysteroscopy only in those patients with a secondary intervention for placental remnants after delivery or patients undergoing a repeat curettage, who develop menstrual disorders.

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