Effects of repeated abdominal paracentesis on uterine and intraovarian haemodynamics and pregnancy outcome in severe ovarian hyperstimulation syndrome

Chin-Der Chen, Jehn-Hsiahn Yang, Kuang-Han Chao, Shee-Uan Chen, Hong-Nerng Ho1 and Yu-Shih Yang

Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan, 100, Republic of China

1To whom correspondence should be addressed at: Department of Obstetrics and Gynecology, National Taiwan University Hospital, 7, Chung-Shan South Road, Taipei, Taiwan, 100, Republic of China

The aims of this study were to investigate the effects of paracentesis on uterine and intraovarian haemodynamics by colour Doppler ultrasound and the influences of repeated paracentesis on pregnancy outcome in severe ovarian hyperstimulation syndrome (OHSS). Forty-one abdominal paracenteses were performed on seven pregnant women with tense ascites and eight thoracocenteses were performed on three pregnant women with pleural effusion. Pulsatility index (PI) and maximum peak systolic velocity (MPSV) of uterine and intraovarian arteries were measured before and after each intervention. The mean PI of uterine arteries was decreased significantly after paracentesis, but not after thoracocentesis. Furthermore, uterine PI was decreased in 13 out of 14 (92.9%) paracenteses with <2500 ml ascites removed, compared with eight out of 13 (61.5%) with >2500 ml ascites removed. After paracentesis, there were no significant changes in the intraovarian PI and MPSV in either group. The 24-hour urine output increased significantly in the paracentesis group, but not in the thoracocentesis group. There were no significant changes in haematocrit and electrolytes as a result of paracentesis. However, gradual falls in serum total proteins and albumin concentrations were observed in all patients after repeated paracentesis, necessitating post-paracentesis albumin infusion. There was no significant difference in miscarriage rates between the two groups. We conclude that repeated abdominal paracentesis increases uterine perfusion and has no adverse effects on pregnancy outcome in severe OHSS. Extraction of 2500 ml of ascitic fluid did not impair uterine perfusion.

Key words: ovarian hyperstimulation syndrome/paracentesis/thoracocentesis/uterine haemodynamics

Introduction

Ovarian hyperstimulation syndrome (OHSS) is a relatively common and potentially life-threatening complication of ovarian stimulation. Its severe form is characterized by massive ascites, marked ovarian enlargement, hydrothorax, oliguria, haemoconcentration and electrolyte disturbance (Rabau et al., 1967). Paracentesis and thoracocentesis have been used to reduce dyspnoea and improve the general condition of patients with tense ascites and pleural effusion (Kingsland et al., 1989; Aboulghar et al., 1993). Most studies concerning paracentesis have dealt with the description of the clinical course as well as the analyses of serum biochemical changes (Thaler et al., 1981; Borenstein et al., 1989; Aboulghar et al., 1993; Shrivastav et al., 1994). No previous study has taken into account the uterine haemodynamic changes after paracentesis in terms of uterine perfusion. An impairment in uterine blood perfusion may be fatal to the conceptus, particularly during early pregnancy. The aims of this study were to investigate the effects of paracentesis on uterine and intraovarian haemodynamics by colour Doppler ultrasound and the influence of repeated paracenteses on pregnancy outcome in severe OHSS.

Materials and methods

Patients

Between August 1996 and September 1997, 20 patients who developed severe OHSS were hospitalized for conservative management. The diagnosis of severe OHSS was based on the classification proposed by Rabau et al. (1967) and modified by Schenker and Weinstein (1978). Conservative management consisted of intravenous fluid plus albumin and a diuretic. Ten of the 20 patients required either paracentesis or thoracocentesis and were enrolled in this study, which was approved by the Ethical Committee of the hospital. Abdominal paracentesis was performed in seven patients who had tense ascites, severe dyspnoea or progressive oliguria, despite conservative treatment. Thoracocentesis was performed in the remaining three women with dyspnoea, who had massive pleural effusion with minimal ascites. Of the 41 paracenteses performed in seven patients, uterine and intraovarian haemodynamic studies were not conducted on 11 occasions. Among the remaining 30 paracenteses, colour Doppler ultrasound failed to detect uterine artery waveform signals before paracentesis in three cases (10%). Overall, 27 paracenteses that had a complete colour Doppler ultrasound study were used for subsequent analysis. All eight thoracocenteses performed in three patients included uterine and intraovarian haemodynamic studies.

Stimulation protocols

The ovarian stimulation protocol for in-vitro fertilization (IVF) using gonadotrophin-releasing hormone agonist (GnRHa) and gonadotrophins has already been described (Chen et al., 1997a). Briefly, pituitary desensitization was initiated using buserelin (Supremon; Hoechst, Frankfurt, Germany) administered by intranasal spray from the midluteal phase of the previous cycle at a dose of 200 µg, four times a day, until the day before transvaginal aspiration of oocytes. Follicle stimulating hormone (FSH) (Metrodin; Serono, Rome, Italy) (150 IU/day) and human menopausal gonadotrophin (HMG) (150 IU/day) were administered twice a day.
Individualized injections of HMG were then continued until the administration of human chorionic gonadotrophin (HCG) (10 000 IU, Profasi; Serono) when two or more follicles had reached a diameter of 18 mm. Transvaginal oocyte retrieval was performed 34–36 h later. Aspirated oocytes were cultured, inseminated or transferred as described (Chen et al., 1997a). The luteal phase was supported with 1500 IU of HCG (Pregnyl; Organon, Oss, The Netherlands) on days 2 and 5 with progesterone in oil, 25 mg daily for 14 days from the day of transfer.

The ovarian stimulation protocol for intrauterine insemination (IUI) consisted of 50–100 mg clomiphene citrate (CC, Serophene; Serono) on cycle days 3 to 7 and HMG, 150 IU/day beginning on cycle day 4 and adjusted to the individual’s response. Monitoring was by transvaginal ultrasound and measurement of serum oestradiol concentrations. When one or more follicles measured $\geq 18$ mm in diameter and the serum oestradiol concentration was appropriate, patients received 5000–10 000 IU HCG, followed by a single IUI 36 h later. Sperm preparations were washed and IUI was performed using techniques described previously (Cheng et al., 1994). The luteal phase was supported with micronized progesterone (Utrogestan; Pierre, Brussels, Belgium), 200 mg daily for 14 days from the day of IUI.

**Assessment of uterine and intraovarian haemodynamics**

All ultrasound examinations were performed using a transabdominal scanhead with colour and pulsed Doppler facilities (Apogee® 800, ATL, Bathell, WA, USA). The spatial peak temporal average intensity of ultrasound for B-mode and Doppler examinations was below 64 mW/cm². Patients were scanned in the supine position, all the scans being performed by the same operator (C.-D.C.). The intra-observer variability for all the measurements was $<11\%$. Only one side of the uterine arteries was measured in order to shorten the examination time and to ensure that the same site of the arteries was sampled after each paracentesis. During each scan, the scanhead was first directed to image the ascending branch of the uterine artery along the lateral border of the uterus. The angle of the transducer was moved to obtain maximum waveform amplitude and clarity. Peak systolic blood flow velocity waveforms were detected and optimal flow velocity waveforms were selected for analysis. The pulsatility index (PI) was calculated according to the formula: $PI = (S - D)/\text{mean}$, where $S$ was the peak systolic shift, $D$ was the minimal diastolic mean, and $\text{mean}$ was the average of the maximum Doppler shifted frequencies over the cardiac cycle. A low value for the PI indicated a decreased impedance to blood flow in the distal vasculature. Once the uterine artery had been assessed, the ovary of the same side was then examined. Flow velocity waveforms were elicited from a main vessel within the ovarian stroma. The lowest PI and the highest maximum peak systolic velocity (MPSV) values were used for statistical analyses. The Doppler examination was repeated after each intervention, taking care to ensure that the sampling sites before and after the intervention were as close as possible. Each examination lasted approximately 20 minutes.

**Abdominal paracentesis and thoracocentesis procedures**

Patients received bed rest before each paracentesis. Ultrasound guidance was used for the identification and localization of fluid in one of the flanks for subsequent paracentesis. An 18-gauge i.v. catheter (Surflo; Terumo, Tokyo, Japan) was introduced into the abdominal cavity without local anaesthesia and connected to a closed drainage system. Ascitic fluid was removed to a maximum of 3500 ml over 20–30 min or until no further fluid could be obtained, though no attempt was made to aspirate totally the ascitic fluid. Vital signs were monitored during and after the procedure. Following paracentesis, albumin (10 g/l of removed ascites) was infused, the dosage being adjusted according to the albumin concentration of the ascitic fluid.

Thoracocentesis was performed by a medical physician under ultrasonic guidance. The pleural effusion was aspirated with a 21-gauge i.v. catheter (Surflo; Terumo), inserted without local anaesthesia into the pleural space through the eighth or ninth intercostal space. Thoracocentesis was continued until no more fluid could be withdrawn, or until respiratory symptoms such as coughing or chest pain developed in the patient.

**Monitoring of patients**

Pulse rate, blood pressure and respiratory rate were monitored immediately before and after paracentesis. After paracentesis, the patients emptied their bladder and began a 24-h urine collection. Blood and ascites samples were obtained for chemical analysis. The same parameters were measured in the thoracocentesis group.

**Hormone assays**

Serum oestradiol and progesterone concentrations were measured using a chemi-illuminencescent immunoassay (Immune assort; D.P.C., Los Angeles, CA, USA). The intra- and interassay coefficients of variation were 6.3% and 6.4%, respectively for oestradiol, and 10.5% and 8.1% for progesterone.

**Statistical analysis**

Results are expressed as means $\pm$ SD. The Mann–Whitney $U$-test was used to compare the differences between groups, and the Wilcoxon signed rank test was used to compare uterine and intraovarian haemodynamic changes before and after an intervention in each group. Fisher’s exact test was used to compare frequencies of observations between groups. Statistical significance was defined as $P < 0.05$.

**Results**

**Clinical and laboratory results**

The clinical and laboratory data of the two groups are presented in Table I. Individual volumes and the mean values of fluid extracted are shown in Figure 1. The mean total volume of ascites removed was 11 740 ml (range 3650–25 900), while the mean total volume of pleural effusion aspirated was 1820 ml (range 1250–2400). The mean time taken for paracentesis was 25 min (range 10–40), and for thoracocentesis was 15 min (range 10–20). The mean hospital stay in the paracentesis group was 27 days (range 17–44), compared with a mean of 11 days in the thoracocentesis group. After an intervention, the pulse rate, blood pressure and respiratory rate showed no significant changes in either group. In contrast, the 24-h urine output was significantly increased in the paracentesis group (from 530 ± 176 ml to 1289 ± 736 ml), but not in the thoracocentesis group (1397 ± 295 ml to 1530 ± 125 ml). Haemocoagulation and electrolyte imbalance were corrected by intravenous fluid therapy before paracentesis in all patients. There were no significant changes in haematocrit or electrolytes as a result of paracentesis. However, gradual falls in serum total proteins and albumin concentrations were observed in all patients after repeated paracentesis, necessitating post-
paracentesis albumin infusion. The median total dosage of albumin per patient was 280 g (range 120–1660).

Uterine and intraovarian haemodynamic measurements

The uterine and intraovarian haemodynamic changes after the interventions are presented in Table II. There were no significant changes in the intraovarian PI and MPSV after the interventions in either group. The mean PI of the uterine arteries was significantly decreased after paracentesis, but not after thoracocentesis. In order to investigate the correlation between the amount of ascitic fluid removed and the uterine haemodynamic changes, the data in the paracentesis group were further analysed by classifying patients as those with >2500 ml (n = 13) and <2500 ml (n = 14) ascites removed. The individual values and means (± SE) of the uterine artery PI before and after paracentesis in the two subgroups are shown in Figure 2. A post-paracentesis decline in uterine PI was seen in 13 out of 14 (92.9%) paracenteses with <2500 ml ascites removed, compared with eight out of 13 (61.5%) with >2500 ml ascites removed. The mean PI of uterine arteries was significantly decreased after the aspiration of <2500 ml ascites, though not in the paracentesis group with >2500 ml ascites removed, or the thoracocentesis group.

Pregnancy outcome

In the paracentesis group, an ultrasound-documented pregnancy was achieved in all seven patients. Six of these pregnancies (85.7%) were multiple pregnancies: five sets of triplets and one twin pregnancy. The only single pregnancy was progressing normally at 29 weeks, while two twin pregnancies were delivered vaginally at term. One triplet pregnancy contained three blighted sacs and uterine evacuation was performed at 8 weeks, while in a second triplet pregnancy the three living fetuses were subsequently lost at 7, 8 and 15 weeks. A third triplet pregnancy contained two blighted sacs and progressed as a single pregnancy to 26 weeks, and a fourth showed evidence of regression of two sacs at 8 and 10 weeks with vaginal bleeding; the patient subsequently delivered a single baby at term. The remaining triplet pregnancy, following elective reduction of one fetus at 10 weeks, delivered twins at 39 weeks.

In the thoracocentesis group, two pregnancies were multiple gestations: one triplet and one twin pregnancy. The twin pregnancy contained one blighted sac which ended in delivery of a full-term baby. The triplet pregnancy, with elective reduction of one fetus at 10 weeks, is currently a twin pregnancy at 30 weeks. The remaining patient had persistent low levels of HCG (maximum, 219 mIU/ml) over 4 weeks, with no sonographic evidence of a gestational sac before 6 weeks, and delivery of a single baby at term. The triplet pregnancy contained two blighted sacs and progressed normally to term, while the remaining triplet pregnancy, following elective reduction of one fetus at 10 weeks, delivered twins at 39 weeks.

Complications of abdominal paracentesis/thoracocentesis

Two patients experienced continuous leakage of ascitic fluid from the puncture sites that were treated successfully by local compression. Injury to the enlarged ovaries or visceral organs did not occur and peritoneal infection did not develop in any patient during or after paracentesis. There were also no complications during or after thoracocentesis.

Discussion

Rabau et al. (1967) were the first to propose abdominal paracentesis for the treatment of OHSS. Paracentesis constitutes the single most important treatment modality in life-threatening situations.
are significantly different; *P < 0.05, paracentesis with pulsatility index (PI) before and after thoracocentesis (m). To our knowledge, this study is the first to investigate the effects of paracentesis on uterine and intraovarian haemodynamics, and demonstrates that drainage of 2500 ml of ascitic fluid within 30 minutes is both safe and beneficial to uterine perfusion. However, the significant increase in uterine perfusion was not consistently observed when >2500 ml of ascites was removed. The reasons for this discrepancy are unknown and could be related to our small sample size, the sensitivity of the colour Doppler ultrasound measurements, or to the hydration status of the patients before paracentesis. It is possible that a colour Doppler waveform study is not sufficiently sensitive to detect the subtle changes in uterine haemodynamics in pregnant women. In addition, rapid mobilization of large volumes of ascitic fluid by paracentesis may be followed by a reduction in the effective intravascular volume (Pozzi et al., 1994), which may cause systemic vessels as well as uterine arteries to contract when a patient is not sufficiently hydrated. Nonetheless, it is important to be aware that the increase in uterine perfusion after paracentesis does not preclude the possibility that such haemodynamic changes could disturb early embryonic implantation, in particular after repeated paracentesis. When considering the aspiration of ascitic fluid in treating severe OHSS, care should be taken not to interfere with embryonic implantation. The miscarriage rate in the paracentesis group of this study was 28.6%, which was not significantly higher than that of other severe OHSS cases treated conservatively (Morris et al., 1995; Balasch et al., 1996; Chen et al., 1997b). In this small series, it appears that there were no adverse effects of repeated paracentesis on early pregnancy in terms of the miscarriage rate.

Total or large volume (4–6 l) paracentesis (Forouzandeh et al., 1996) has been frequently used to treat patients with cirrhosis of the liver and refractory ascites. Haemodynamic studies in cirrhotic patients with ascites have shown that a significant reduction of intravascular volume occurs more commonly when the ascitic fluid is totally mobilized without plasma volume expansion (Pozzi et al., 1994). We did not aim to aspirate the ascitic fluid completely, as this would cause a significant protein loss that would require intravenous albumin infusion after paracentesis. In animal studies, it has been shown that albumin gene expression is down-regulated by infusion of albumin (Pietrangelo et al., 1992); therefore, at least theoretically, albumin as a plasma volume expander might contribute further to the hypoproduction of albumin. This is

| Table II. Uterine and intraovarian haemodynamic changes in patients undergoing paracentesis and thoracocentesis |
|---------------------------------------------------------------|---------------|
|                                                               | Paracentesis group (n = 27) | Thoracocentesis group (n = 8) |
|                                                               | Before | After | Before | After |
| **Uterine artery**                                            |        |       |        |       |
| PI                                                             | 1.27 ± 0.38a | 1.19 ± 0.39a | 1.51 ± 0.20 | 1.47 ± 0.13 |
| MPSV                                                           | 0.33 ± 0.08 | 0.34 ± 0.07 | 0.36 ± 0.10 | 0.37 ± 0.18 |
| **Intraovarian artery**                                       |        |       |        |       |
| PI                                                             | 0.70 ± 0.12 | 0.69 ± 0.11 | 0.75 ± 0.12 | 0.74 ± 0.13 |
| MPSV                                                           | 0.30 ± 0.07 | 0.29 ± 0.09 | 0.28 ± 0.07 | 0.29 ± 0.06 |

Results are expressed as mean ± SD. Results are significantly different (P < 0.028, Wilcoxon signed rank test).
PI = pulsatility index; MPSV = maximum peak systolic velocity.

Figure 2. Individual values and means (± SE) of the uterine artery pulsatility index (PI) before and after thoracocentesis (♀) (n = 8), paracentesis with >2500 ml ascites removed (●) (n = 13), and paracentesis with <2500 ml ascites removed (○) (n = 14). Results are significantly different; *P = 0.011, Wilcoxon signed rank test.

OHSS not controlled by medical therapy (Padilla et al., 1990). The physiological basis of this approach is derived from studies of liver cirrhosis patients with tense ascites. In these patients, drainage of the abdominal fluid presumably decreased intra-abdominal pressure, thereby improving venous return, cardiac output and renal perfusion (Forouzandeh et al., 1996). Some groups do not recommend paracentesis at all because of the danger of puncture and laceration of enlarged ovarian cysts (Schenker and Weinstein, 1978). However, by using ultrasound guidance, the procedure can be applied safely and the risk of puncturing a cyst is minimized (Runyon, 1986).

All patients in the paracentesis group of this study conceived and required repeated paracentesis, representing a group of patients with life-threatening OHSS. Because impairment in uterine blood perfusion could be fatal to the conceptus (Tekay et al., 1996), it was very important to investigate whether repeated paracentesis would impair uterine perfusion, especially during early pregnancy. To our knowledge, this study is
especially important as a large number of our patients became pregnant and it is not appropriate to initiate a pregnancy in a protein-depleted state. In cirrhotic patients with tense ascites and peripheral oedema, <5 l of ascitic fluid can be safely removed without administering a plasma volume expander. However, the optimal amount of ascites removed from pregnant women with severe OHSS is open to debate. Our experience showed that a marked relief of compression symptoms occurred after removing the first 1000 ml of ascitic fluid. However, incomplete tapping might result in rapid re-collection of ascites, requiring re-tapping. The more times paracentesis is carried out, the greater the risk of complications occurring. Recently, Al-Ramahi et al. (1997) reported three cases when an indwelling peritoneal catheter was used to decrease the need for repeated paracentesis. The authors concluded that continuous drainage of the ascitic fluid is a better alternative to multiple abdominal paracentesis in the management of severe OHSS.

We are aware that our study has two limitations. First, it was not a randomized controlled trial and thus it was impossible to know definitely whether the improvement observed in our cases was the result of therapy or merely the consequence of the natural course of the syndrome. On the other hand, all of our patients presented with life-threatening OHSS. It is inappropriate to enrol as controls patients who can be treated conservatively, since they represent a different group of patients without life-threatening OHSS. Likewise, it is ethically unacceptable to include as controls patients with untreated life-threatening OHSS. Secondly, while uterine artery blood flow can be assessed by means of colour Doppler ultrasound with sufficient reproducibility (Steer et al., 1995), the most important issue is whether the same vessel is sampled on each occasion. It is possible that adjacent branches or vessels were sampled and that differences in PI resulted from different sites being measured. Indeed, the positional change of the uterus and ovaries after ascites aspiration has made precise localization of the sampling site difficult. Furthermore, a change in uterine position may have affected uterine artery blood flow (Dickey et al., 1994).

In conclusion, repeated abdominal paracentesis increases uterine perfusion and has no adverse effects on the pregnancy outcome in severe OHSS in terms of the miscarriage rate. Extraction of 2500 ml of ascitic fluid is possible without impairing uterine perfusion. However, further study is needed before definite guidance can be given regarding routine paracentesis in pregnant women with severe OHSS.

References


Received on January 27, 1998; accepted on May 18, 1998

Paracentesis for treatment of severe OHSS

2081