APPRAOCH TO THE TREATMENT OF ASCITES ASSOCIATED WITH OVARIAN HYPERSTIMULATION SYNDROME

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Abstract: Ovarian hyperstimulation syndrome (OHSS) is almost cases an iatrogenic complication. Severe OHSS is characterised by ovarian enlargement, ascites, electrolyte imbalance, hypovolemia, and hemoconcentration. The pathophysiologic factors of this syndrome are not well known.

It has been observed that paracentesis is efficacious, provided that care is taken to reinfuse protein lost in the peritoneal exudate. For this reason, in two patients with severe OHSS, we used a dialytic technique of reinfusing concentrated ascitic fluid. Here, we report two cases of severe OHSS following IVF with massive ascites in which we reinfused concentrated ascites by ultrafiltration.

Through sonography-guided paracentesis, the ascitic fluid was concentrated by ultrafiltration and reinfused. The concentrated fluid was returned to the peripheral vein. In these patients, a progressive increase of diuresis was evident during treatment and subjective improvement was almost immediate. After treatment, hematologic and biochemical parameters had returned to normal limits. In treating severe OHSS, we have used the technique of reinfusing of concentrated ascitic fluid to avoid protein depletion induced by paracentesis. We were able to successfully restore to normal the hematological and biochemical imbalance with one treatment. Treatment of OHSS with this ultrafiltration and reinfusion method may help to resolve serious cases of OHSS and to treat severe OHSS.

Key words: Ascites, Ovarian hyperstimulation syndrome, Paracentesis

INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is the most serious complication of ovulation induction with exogenous gonadotropins, such as human menopausal gonadotropin and follicle-stimulating hormone. These hormones are considered to increase capillary permeability and cause a third space fluid shift. OHSS is a threat to every woman undergoing ovulation induction and is potentially lethal in its severest form. Severe OHSS is characterized by the growth of multiple large follicles with a massive extravascular protein rich fluid shift. This may lead to hypovolaemia, haemoconcentration, oliguria, and electrolyte disturbance. Human albumin solutions are now used in the management of shock and other conditions in which restoration of blood volume is urgent, as well as in the acute management of burns and clinical situations associated with hypoproteinaemia.

Recently, a number of clinical trials with conflicting results have been reported in which reinfusion of concentrated ascitic fluid is done as a possible way to prevent the severe form of OHSS. Here, we report two cases of severe OHSS following in-vitro fertilization (IVF) with massive ascites in which we reinfused concentrated ascites by ultrafiltration.
MATERIALS AND METHODS

All patients were referred to the Department of Obstetrics and Gynecology Gunma University School of Medicine, as outpatients for evaluation and treatment by assisted reproductive technologies between January and June 2000. Over the 6 month period, 128 patients underwent IVF-embryo transfer and 6 patients (4.7%) were considered to have severe OHSS. Severe OHSS was diagnosed in the presence of marked ascites in the upper abdomen by at least one of the following laboratory data criteria: hemoconcentration (hematocrit > 45%), hypoproteinaemia (serum total protein < 6.0 g/dl), and hypoalbuminaemia (serum albumin < 3.5 g/dl) and based on ovarian enlargement (> 10 cm in diameter). Two of 6 patients had undergone reinfusion of concentrated ascites by ultrafiltration.

Reinfusion system for ascites with concentration by ultrafiltration. (Figure 1)

A 16-gauge teflon catheter was placed under the ultrasonic guidance, into the peritoneal cavity and ascites were stored. Through a peristaltic pump (PRS-20, Nikkiso, Tokyo, Japan) and micro-filter (AHF-MO; diameter of the pore, 0.2 μm, Asahi medical, Tokyo, Japan), filtrated ascites was connected to a concentrated machine (AHF-UNH; Asahi medical, Tokyo, Japan). With an 18-gauge Teflon catheter inserted into the antecubital vein, reinfusion of concentrated ascites was performed once a day for 5 h at a rate of 100-200 ml/h.

CASE 1

A 24 year old nulligravid patient with 2 years of primary infertility due to male factor was treated by IVF-embryo transfer. After down regulation and suppression had been achieved using a gonadotropin releasing hormone analogue (GnRHα), human menopausal gonadotropin (HMG Pergoreen; Serono Japan, Tokyo, Japan) 150 IU/day i.m and pure follicle-stimulating hormone (pFSH Fertinorm P; Serono Japan, Tokyo, Japan) 75 IU/day i.m. were administered. Five ampoules of HMG and 18 ampoules of pFSH were given and human chorionic gonadotropin (HCG Pregnyl; Organon Japan, Tokyo, Japan) 10000 IU s.c. was administered on day 12 of HMG. At the time of HCG, a transvaginal ultrasound showed eight follicles > 16 mm, and 14 follicles < 16 mm mean follicular diameter. A transvaginal ultrasound guided oocyte retrieval was performed 34 h after HCG administration. Thirteen oocytes were obtained from the left ovary. All of embryo was not transferred and it was frozen after ovum pick-up (OPU). The patient complained of abdominal swelling, nausea, vomiting, and showed 3 kg weight gain over 2 days. She was admitted and treated for OHSS. On examination at admission her pulse was 110/min and blood pressure 110/69 mmHg. The pulmonary sound was clear, the abdomen was distended, the ovaries were enlarged and ascites was present. She was rehydrated with normal saline 60 ml/h i.v., 25% albumin solution at 100 ml/day, and started on heparin 2500 i.v. After 3 days, a weight gain was noted with increasing abdominal girth and massive ascites. Laboratory tests revealed hemoglobin 16.1 g/dl, hematocrit 46.7%, white blood cell concentration of 16400/μl. The electrolyte concentrations were: sodium 136 mEq/l, potassium 4.3 mEq/l, albumin 3.7 g/dl, total protein 5.9 g/dl. Under ultrasound guidance, we performed paracentesis and reinfusion of concentrated ascites by ultrafiltration. After recirculation of ascites, the patient had less abdominal discomfort and a decrease in the abdominal girth and a weight with normal urine output. Neither complication nor adverse reactions was found. Severe OHSS resolved after 14 days and the patient was discharged in good condition. Clinical labo data transition and treatment during OHSS are shown in figure 2.

CASE 2

A 27 year old nulligravid patient with 2 years of primary infertility due to male factor was treated by IVF-embryo transfer. In the short protocol, using GnRHα, HMG 150 IU/day i.m. was administered. A total of 9 ampoules of HMG was given until follicular maturation was achieved and HCG 10000 IU s.c. was administered on day 11. At the time of HCG, a leading follicle reached 16 mm in diameter. Twenty six oocytes were obtained and total of sixteen oocytes fertilized. All of embryo was not transferred and it was frozen. The patient complained of abdominal swelling, nau-
The treatment of ovarian hyperstimulation syndrome

Case 1

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<th>Human albumin (25% 100ml)</th>
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<td>Low-molecular weight heparin 2500U/day</td>
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Fig. 2 Clinical treatment course and laboratory parameters of the patient presented after ovum pick-up (OPU)

Case 2

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Fig. 3 Clinical treatment course and laboratory parameters of the patient presented after ovum pick-up (OPU)

sea, vomiting, ovarian enlargement (10cm in diameter), one day after OPU and showed 3.5kg weight gain over 2 days. She was admitted and rehydrated with normal saline 60mL/L i.v., 25% albumin solution at 100mL/day and started on heparin 2500/day i.v. After a few days, a weight gain was noted with increasing abdominal swelling and massive ascites. After recirculation of ascites had been done in two course, the patient had less abdominal discomfort and a decrease in abdominal swelling and weight with a normal urine output. Neither complication nor adverse reaction was found. Severe OHSS resolved after 19 days. The clinical labo data transition and treatment during the OHSS are shown in figure 3.

**DISCUSSION**

The frequency of OHSS has increased with the increased use of ovulation agents necessary for ovarian stimulation in assisted reproductive technology therapy including IVF-embryo transfer. Although the pathogenesis of OHSS is still unclear, several chemical mediators are found in large amounts in ascites. It is believed that stimulation of the ovarian renin-angiotensin system plays a part. It has been suggested
that the presence of high concentration of angiotensin II like substance leads to vasodilatation and increased capillary permeability. The chemical mediators that are considered to cause and prolong clinical conditions of OHSS may be numerous in the ascitic fluid\textsuperscript{13}. The increase in capillary permeability leads to a shift of fluid to the third space compartments, mainly the peritoneal cavity with the formation of ascites. Massive ascites can lead to severe abdominal distention and dyspnea. When patients present abdominal distention and oliguria, paracentesis relieves the symptoms and changes the course of illness. However, the removal of a large amount of ascites decrease the intraabdominal pressure caused by paracentesis, which may facilitate shifting of fluid from the intravascular compartment to the peritoneal cavity, with a rapid reaccumulation of ascites and a decrease of the effective intravascular volume\textsuperscript{4,10}.

Reinfusion of concentrated ascites by ultrafiltration may decrease the chemical mediators causing OHSS, and increase the plasma penetration pressure and resultant revision of the fluid imbalance. Simple ascites drainage and albumin infusion which is the standard treatment for severe OHSS could be performed, but it does not lead to shortening of the clinical course of OHSS. Recirculation of ascites in patients with OHSS shortens the clinical course and improves the clinical conditions of OHSS. It is also an easy procedure. Reinfusion of concentrated ascites by ultrafiltration is expected to overcome these problems including present one.

In conclusion, the reinfusion of concentrated ascites by ultrafiltration makes it possible to maintain the serum protein concentration and expedite prompt recovery from severe OHSS.

REFERENCES