

Does intravenous administration of human albumin prevent severe ovarian hyperstimulation syndrome?

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Objective: To report our experience with IV albumin as a means to prevent ovarian hyperstimulation syndrome (OHSS) in high-risk patients.

Design: Retrospective case-series.

Setting: University hospital-based IVF program.

Patients: Five women undergoing controlled ovarian stimulation for IVF. Based on previous history and/or E_2 measurements and number of ovarian follicles, these patients were considered to be at high risk for developing OHSS.

Interventions: Intravenous albumin was given at the time of oocyte retrieval. Additional doses were given 12 and 24 hours later.

Main Outcome Measure: Development of OHSS.

Results: Four patients developed OHSS; two of them had the severe form of the syndrome.

Conclusions: Severe OHSS may develop in high-risk patients despite the prophylactic administration of IV albumin. *Fertil Steril*® 1996;66:654-6

Key Words: Human albumin, ovarian hyperstimulation syndrome, IVF, ovulation induction, high risk subjects

Ovarian hyperstimulation syndrome (OHSS) is one of the most serious complications of ovulation induction with gonadotropins. Although some of the risk factors of OHSS are known, it is not always possible to predict its occurrence. Several approaches have been suggested in the context of preventing OHSS or minimizing its severity (e.g., stimulation with low doses of gonadotropins, use of low-dose mid-cycle hCG, avoiding hCG for luteal support, avoiding ET, and use of GnRH agonist (GnRH-a) for triggering LH surge). Of special interest are reports by

Asch et al. (1) and Shoham et al. (2), who successfully prevented OHSS in high-risk patients by the administration of human albumin. A total of 52 cases were reported by both groups, without a single case of OHSS. In view of these reports, we have tried this approach in five patients, however, the results were less than encouraging.

CASE REPORTS

In all five patients, ovarian stimulation was initiated with FSH and hMG after pituitary down-regulation with midluteal GnRH-a (3.75 mg Decapeptyl CR [D-Trp6 LHRH]; Ferring, Malmo, Sweden). Stimulation was monitored by daily measurements of serum E_2 and P levels and by sonography on day 3 (baseline) and daily from day 6 of treatment. Ovu-

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lation was triggered by 10,000 IU hCG when at least two of the leading follicles reached a diameter of 16 mm. Oocytes were retrieved transvaginally 34 to 36 hours later. We decided to use albumin in patients with a history of previous OHSS, high E₂ (>3,600 pg/mL [13,200 pmol/L]) on the day of hCG administration, and a large number of growing follicles. Consequently, the E₂ levels ranged between 3,814 and 7,404 pg/mL (14,000 and 27,180 pmol/L; mean, 5,402 pg/mL), and the number of retrieved oocytes ranged between 26 and 47 (mean, 33). Patients' clinical profiles are summarized in Table 1. Ascites was found in all five patients and was graded as "minimal" (peritoneal fluid is localized to the pelvic area as shown by sonography, no clinical signs), "moderate" (peritoneal fluid is demonstrated in the pelvic area and in upper abdominal region [hepatorenal pouch], abdominal distention is evident), and "severe" (large amount of peritoneal fluid causing tense abdominal skin). Dyspnea was graded as "no" (no symptoms, respiratory rate < 15/min), "mild" (tachypnea [15 to 20/min], patient complaining of mild discomfort), and "severe" (tachypnea [>20/min], patient complaining of severe shortness of breath and discomfort). Albumin (Human Albumin, 25%; Kamada, Kibbutz Beit Kama, Israel) was given immediately after retrieval and was repeated 12 and 24 hours later. In three patients, a total dose of 37.5 g was given. We increased the dose to 75 g when two of these patients developed OHSS. The two patients who received the higher dose of albumin (75 g) developed signs and symptoms of OHSS within 48 hours after oocyte retrieval. Embryo transfer was withheld, nevertheless, OHSS progressed to its severe form, leading to intensive care measures and repeated aspiration of ascitic fluid. In two patients, signs and symptoms included considerable amount

of ascitic fluid and dyspnea in one patient, however, no interventions were warranted other than hospitalization for observation. The fifth patient did not develop OHSS.

DISCUSSION

In light of very encouraging reports on the successful use of albumin in an effort to prevent OHSS (1, 2), we have used this approach in a small group of five high-risk patients. Our results are disappointing, as two patients developed very severe OHSS. This limited series of patients adds to an additional report describing the development of severe OHSS in two patients despite prophylactic albumin (3). Notably, the inclusion criteria for a "high-risk" patient are not identical in the successful series (1, 2). In fact, the mean E₂ level and number of oocytes retrieved are clearly higher in our series compared with that of Shoham et al. (2). That notwithstanding, the occurrence and severity of OHSS do not correlate directly with these variables.

Of interest is the fact that two patients developed severe OHSS despite withholding ET. This observation clearly demonstrates that severe OHSS can develop in patients given a large dose of albumin, despite the lack of subsequent ongoing pregnancy.

We chose to administer albumin in three doses over a 24-hour period because we felt that the continuous pouring of "vasoactive substances" from the ovaries would be better met by repeated doses. Although previous published reports favored a single 50-g dose, of note is the fact that severe OHSS developed in the two patients that received 75 g of albumin.

The proposed mechanism by which albumin may prevent OHSS emphasizes its ability to maintain

Table 1 Patients Clinical Profiles

Patient	E ₂ * pg/mL	Previous OHSS	No. of oocytes	Albumin given g	Ascites	Dyspnea	Pleural† effusion	Oliguria‡	Hemoconcentration§
1	3,814	+	28	75	Massive	Severe	Yes	Yes	Yes
2	7,300	-	36	75	Massive	Severe	Yes	Yes	Yes
3	7,404	-	47	37.5	Moderate	No	No	No	No
4	4,650	-	30	37.5	Moderate	Mild	No	No	No
5	3,841	-	26	37.5	Minimal	No	No	No	No

* On day of hCG administration. Conversion factor to SI unit, 3.671.

† Pleural effusion was diagnosed by chest roentgenogram.

‡ Oliguria was defined as urine output < 600 mL/24 h.

§ Hemoconcentration was defined as hematocrit ≥ 45%.

|| All embryos were cryopreserved.

plasma oncotic pressure and to bind putative active compounds secreted by the ovaries, thereby reducing their free (active) component. Because the pathogenesis of OHSS, as well as the putative way by which albumin may prevent it, are not completely understood, consideration should be given to the possibility that the stimulated ovaries may secrete mediators that are not affected by albumin. Although albumin could have contributed to reducing the severity of the syndrome in our limited series, it is far from being a panacea in the context of OHSS. A large-scale prospective study should be conducted to allow for a meaningful conclusion.

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