Continuous Intravenous Albumin Prevents Hemoconcentration, Hypercoagulability and Hypoalbuminemia but not Ascites in Severe Ovarian Hyperstimulation Syndrome "A report of two cases"

DEVAMLI İNTRAVENÖZ ALBUMIN İNFÜZYONU AĞIR OVARYAN HİPERSTİMÜLASYON SENDROMUNDA HEMOKONSANTRASYONU HİPERKOAGÜLEBİLİTEYİ VE HİPOALBUMİNEMİYİ ÖNLEMEKTE ANCAK ASCIT'İ ÖNLEYEMEMEKTEDİR 'İKİ VAKA SUNUMU'

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Summary

Objective: *Under continuous intervenous ulhumin treatment, we evaluate two cases with massive ascites, but without hemoconcentration, hypercoagulability and hypoalbuminemia are described in the present study with the mechanisms oj current understanding.*

Institution: *Gülhanc Military Medical Academy Department of Obstetrics and Gynecology.*

Material and Methods: *Two cases with high risk for OHSS (enlarged ovaries and E2 more than 3000pg/ml on the day of HCG) 5(lg of Human albumin (200ml of%25 albumin in iv over 60 minutes) was infused continuously betwen the time of oocyte retrieval and embryo transfer.And followed by a standing dose of 12.5g every 4 hours.Intravenous fluid therapy and transvaginal aspiration ofascitic fluid were administirated as adjuvant treatment to prevent the deterioration of the situation.Human Albumin was infused for 7 days in the standing dose because of severe OHSS.*

Results: *In both cases continuous intravenous albumin prevent hemoconcentration, hypercoagulability, hypovolemia-oliguria and hypoalbuminemia despite massive ascites, correction of increased capillary permability seems to be the main necessity to prevent or treat severe OHSS.Continuous use of intravenous human albumin may give us an apporlunity to prevent the lethal complications due to hypovolemia.*

Key Words: Human albumin, Severe OHSS

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Özet

Amaç: *Bu çalışmada sürekli intraveıiöz albümin uygulanan masif ascitesli ancak hemokonsantrasyon, hiperkoagülabilite ve hipoalbıuminemi gelişmeyen iki olgu eldeki bilgiler ışığında değerlendirildi.*

Çalışmanın Yapıldığı Yer: *Gülhane Askeri Tıp Akademisi Kadın Hastalıkları ve Doğum Arıabilim Dalı.*

Materyal ve Metod : OHSS için risk altında olan (genişlemiş överler ve HCG gününde 3000pg/ml nin üzerinde E2) iki vakaya oosit toplama ve eıiıbrio transferi zamanları arasında 50 gr. devamlı Humarı albumin infüzyonu (60 dk'da %25 lik albuminden 200 cc) yapılnıştır.Dalıa sonra 4 saate bir 12.5 gr lık idame dozuna geçilmişlir.Haslanırı durumunun kötüleşmemesi için adjuvan tedavi olarak intraveıiöz sıvı replasınanı ve iransvaginal ascit aspirasyonıı yapılmıştır.Şiddetli OHSS nedeniyle Humarı Albumin infüzyoıiuıia idame dozunda 7 gün devam edilmiştir.

Sonuçlar *: Her iki vakada da sürekli intraveıiöz albumin infüzyonu heırıokonsantrasyonu, hiperkoagülebiliteyi, hipovolemi-oligüri ve hipoalbuminemiyi öıilemit ancak şiddetli asciti önleyememiştir. Artmış kapıller permeabilitenin düzeltilmesinin şiddetli OHSS nin önlenmesinde ve tedavisindeki temel gereklilik gibi görülmektedir. Sürekli uygulanan intraveıiöz humaıı albumin, hıpovolemiye bağlı ölümcül komplikasyorıların önlenmesinde bize bir fırsat tanımaktadır.*

Anahtar Kelimeler : İnsan albumini, Ciddi OHSS

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Severe ovarian hyperstimulation syndrome (OHSS) is mainly characterized by enlarged ovaries, hypovolemia-electrolyte imbalance, hemoconcentration-hypercoagulability and third space

accumulation of fluid in the form of ascites, pleural and pericardial effusion. Incidence of severe OHSS was reported as 0.5% among patients undergoing controlled ovarian hyperstimulation (COH) and no unique method to prevent OHSS has been described (1).

Single dose human albumin has been suggested to prevent OHSS by binding the factors that are responsible for increased capillary permeability in two series (2,3). Recently, severe OHSS despite single dose prophylactic albumin at the time of oocyte retrieval was reported in two cases undergoing in vitro fertilization and embryo transfer (IVF-ET) (4). So we decided to use intravenous albumin continuously between the time of oocyte retrieval and embryo transfer. In the present study, the outcome of this new approach in first two cases are discussed.

Case reports

Case I

A thirty-year old woman with primary infertility due to polycystic ovarian disease (PCOD) was induced with long protocol Buserelin 900 mg/day (Suprcfact nasal spray Hoechst/Germany) and low-dose step-up pure FSH (Metrodin amp./Serono S.A./Switzerland). Her day 3 FSH and E2 were <10 mlU/ml. and <20 pg/ml. respectively. A total of 25 ampules of pure FSH were administered in 12 days. On the day of hCG, E2 was 3650 pg/ml., so 5000 III of hCG (Profasi amp./Serono) were administered. Both ovaries were measured as 8X9 cm. on the day of hCG. Forty-two oocytes were aspirated via transvaginal ultrasonographic guidance under local anesthesia. At retrieval, 50 g. of human albumin (200 ml. of 25% albumin IV., over 60 minutes) (Plasbumin -25, Miles Inc./Canada) was infused, and followed by a standing dose of 12.5 g. every 4 hours in the clinic since the patient had significant risk for OHSS. Three days after retrieval four embryos were transferred and micronized progesteron (Utrogestan 100 mg/cap./ Laboratoires BESINS ISCOVESCO - PARIS) 600 mg/day was administered vaginally for luteal support.

On the day of ET the patient had abdominal distention and the ovaries were measured as 12X12 cm. with massive ascites. Lactated Ringer's solution was infused 1000 ml. daily, and transvaginal aspiration of ascites was performed on post ET days 2, 3 and 4. Human albumin was infused for 7 days in the standing dose because of severe OHSS. Daily parameters for management were summarized in Table 1. Significant increases in creatininemia, BUN and leukocytes were found. Hematocrit was slightly increased but returned to normal on post ET day 6. Prothrombin time was not changed. Urinary output was maintained despite high creatininemia and BUN throughout the treatment. Bilirubinemia, ALT and AST was not changed. The ascites with abdominal distention was resolved on post ET day 7 and the patient was discharged home. Pregnancy test with serum b-hCG was measured as 140 mlU/ml. on post ET day 12.

Case II

The second patient was a 28 year-old woman with primary unexplained infertility, and she was induced with Buserelin long protocol plus pure FSH and hMG (Pergonal amp./Serono/

Tab I nmary of parameters for management in both cases.

	Hie		Leukocyte (mm 3)		Creatininen)«! (mg/dl)		BUN (mg/dl)		Albumtnemia (mg/dl)		Prothrombin time (s)		Ascites aspirated (ml)	
	Case 1	Case 2	Case 1	Case 2	Case I	Case 2	Case 1	Case 2	Case 1	Case 2	Case 1	Case 2	Case 1	Case 2
H C G day	35.6	32.0	11400	9600	0.6	0.7	29	33	3.9	4.2				
OP day	34.4	32.3	-		0.8		27	.	3.8		11.6	11,9		
ET day	37,7	34.1		-	1.1	1,2	42	45	4.1	4.0				
Post HT day I	39. i	34,2	15100	11600	2.0	1.4	61	48	3.9	3.9	11.8			
Post E T day 2	.39.5	33.8	26300	12100	2.4	1.5	62	41	3,7	3.9		11.8	1500	1500
Post HT day 3	39,5	33,6	19300	12400	3.0	1.3	75	36	3.5	4.1			1500	1500
Post ET day 4	38,3	32.5	Î8600	10700	3,3	1.1	89	35	.3,0	4.3	11.8		1500	
Post BT day 5	38.4	32,5	15400	9100	2.2	0,9	64	26	.3,4	4,3				
Post HI' day 6	37,6		12700		1.3		45		3,6					
Post ET day 7	36.4		11.300		1.1		33		4.1					

Switzerland). Her day 3 FSH and E2 were <10 mlU/ml. and <20 pg/ml. respectively. A total of 27 ampules of gonadotropins were administered in 10 days. On the day of hCG, E2 was 3100 pg/ml, so 5000 1U of hCG were administered. Both ovaries were measured as 7X8 cm. on the day of hCG. Twenty-seven oocytes were collected via transvaginal ultrasonographic guidance under local anesthesia. At retrieval 50 g. of human albumin (200 ml. of 25% albumin IV over 60 minutes) (Plasbumin -25, Miles Inc./Canada) was infused, and followed by a standing dose of 12.5 g. every 4 hours in the clinic because of risk for OHSS. Three days after retrieval four embryos were transferred. Luteal support was administered as vaginal micronized progesteron 600 mg/day. On the day of ET the ovaries were measured as 10X10 cm. with massive ascites. Lactated Ringer's solution was infused 1000 ml. daily, and transvaginal aspiration of ascites was performed on post ET days 2 and 3. Human albumin was infused for 7 days in the standing dose because of severe OHSS.

Daily parameters for management were summarized in table I. Slight increases in hematocrit, creatininemia, BUN and leukocytes were encountered. Urinary output, prothrombin time, and liver enzymes were not changed. The ascites with abdominal distention was resolved on post ET day 7 and the patient was discharged home. Pregnancy test with scrum b-hCG was measured as 5 mlU/ml. on post ET day 12.

Discussion

Single dose 50 g. of human albumin at retrieval was used to prevent severe OHSS in high risk patients. The rationale for this hypothesis was that albumin could bind the factors that are responsible for the increased capillary permeability (2,3). In a recent report of two cases, severe OHSS has been shown despite prophylactic albumin at retrieval (4). Moreover, in this case report, human albumin was used as the only means to treat hypovolemia and hemoconcentration of the patients at second admission.

So the present study was conducted in patients with high risk for OHSS (ie, enlarged ovaries and E2 more than 3000 pg/ml on the day of hCG). Human albumin was infused continuously between the time of oocyte retrieval and embryo transfer. Since massive ascites was encountered on the day of ET, human albumin infusion was continued until significant well-being. Moreover, intravenous fluid therapy and transvaginal aspiration of ascitic fluid were administrated as adjuvant treatment to prevent the deterioration of the situation.

Aspiration of ascitic fluid and intensive intravenous fluid therapy was found to correct the hcmoconcentration-hypercoagulability and hypovolemia-oliguria-electrolyte imbalance in 24 hours after aspiration interestingly (5).

For our cases, intravenous daily 50 g. of human albumin was used continuously between retrieval day and resolution of ascites. Lactated Ringer's solution 1000 ml. was infused daily and transvaginal aspiration of ascitic fluid was performed for 2 or 3 times.

The main outcome of continuous intravenous albumin therapy was prevention of hemoconcentration-hypercoagulability, hypovolemia-oliguria and hypoalbuminemia despite massive ascites. In our understanding, albumin has its most important effect in the correction of oncotic pressure, rather than increased capillary permeability since it can not prevent formation of ascites despite continuous administiration.

Aspiration of the ascitic fluid, in our cases, did not cause a dramatic change in parameters of management. However, this palliative approach corrects the patient's comfort by reducing intrabdominal pressure and distention.

Another important aspect of the study is that one of the patients has become pregnant while the other has not. So the endogenous hCG might only slightly contribute to the condition.

As for conclusion, correction of increased capillary permeability seems to be the main necessity to prevent or treat severe OHSS. Continuous use of intravenous albumin may give us an opportunity to prevent the lethal complications due to hypovolemia.

REFERENCES

1. **Navot D, Bcrgh PA, Laufer N. Ovarian hyperstimulation syndrome in novel reproductive technologies : prevention and treatment. Fértil Steril 1992; 58 : 249-61.**

2. Asch RH, Ivery G, Gokisman M, Fredrick JL, Stone SC, Balmaceda JR The use of intravenous albumin in patients at high risk for severe ovarian hyperstimulation syndrome. Human Reproduction 1993 ; 8:1015-20.

3. Shoham Z, Weissman A, Barash A, Borenstein R, Schachter M. Insler V. Intravenous albumin for the prevention of severe ovarian hyperstimulation syndrome in an in vitro fertilization program : a prospective, randomized, placebo-controlled study. Fertil Steril 1994 ; 62 : 137-42.

4. Mukherjee T, Copperman AB, Sandler B, Bustillo M, Grunfeld L. Severe ovarian hyperstimulation despite prophylactic albumin at the time of oocyte retrieval for in vitro fertilization and embryo transfer. Fertil Steril 1995; 64 : 641-3.

5. Aboulghar MA, Mansour RT, Serour G1, Sattar M, Amin Y, Elattar 1. Management of severe ovarian hyperstimulation syndrome by ascitic fluid aspiration and intensive fluid therapy. Obstetrics and Gynecology 1993 ; 81: 108-11.