Retrospective Analysis of Human Serum Albumin use From Gynecologic and Obstetric Point of View

Jinekoloji ve Obstetri Bakış Açısı ile İnsan Serum Albumin Kullanımının Retrospektif Analizi

İnsan Serum Albumin Kullanımı / Human Serum Albumin Use

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Özet

Amaç: İnsan serum albumini (İSA] dolaşım sisteminde bulunan en belirgin proteindir. İSA, koloid solüsyon olarak özellikle yoğun bakım ünitelerinde birçok endikasyonla yaygın olarak kullanılmaktadır. Birçok endikasyonu olmasına rağmen günlük kullanımda uygunsuz endikasyonlara sıklıkla rastlenmaktadır. Jinekoloji ve obsterti de çeşitli endikasyonlarla İSA kullanımının sık olduğu bir branştır. Uygunsuz kullanımının yanında, yüksek maliyeti, teorik hastalık bulaş riski, daha az maliyetli alternatiflerinin de bulunduğu göz önüne alındığında, bu çalışmamızda Sağlık bakanlığının İSA kullanım yönergesi ışığında üçüncğ basamak dal hastanesi olan hastanemizin verilerini kullanarak, jinekoloji pratiğinde İSA kullanımı ve kullanım endikasyonlarındakideğişiklikleri değerlendirmeyi amaçladık. Gereç ve Yöntem: Çalışma için hastanemiz bilgi işlem sisteminden perinatoloji, jinekolojik onkoloji ve reprodüktif endokrinoloji kliniklerindeki HSA kullanım oranları ve kullanım endikasyonları incelendi. 2012 yılı sonunda Sağlık Bakanlığı tarafından yayınlanan İSA kullanımı ile ilgili yönerge öncesi İSA kullanım sıklığı ve kullanım endikasyonlarındaki değişiklikler istatistiksel olarak karşılaştırıldı. Bulgular: Perinatoloji kliniğinde 2012 yılında Albumin kullanımı doğum başına 0,0027 iken bu oran 2013 yılında 0,018'e gerilemiştir. Yönerge sonrası İSA kullanımı artan tek kliniğin jinekolojik onkoloji olduğu gözlenmiştir. Tartışma: Jinekolojik onkoloji hariç diğer kliniklede HSA kullanım oranında bir azalma göze çarpmakla birlikte, endikasyon dışı kullanım oranı halen yüksek düzeylerdedir. Uygun endikasyonların özümsenmesi ve günlük pratikte uygulamaya geçirilebilmesi jinekologlar arasında kliniklerinde uygun tedavi verilebilmesi için önem taşımaktadır.

Anahtar Kelimeler

İnsan Serum aLbumini; Jinekoloji ve Obstetri; Hipoalbuminemi; İSA

Abstract

Aim: Human serum albumin (HSA) is the most abundant circulating protein in the body. HSA, as a colloid solution, used for several conditions in daily clinical practice especially in intensive care units. HSA is commonly used for several indications but its administration could often be considered as inappropriate. Gynecology and obstetrics is an important specialty that HAS administration is necessary for several different conditions. Beside the proportion of inappropriate use, the elevated cost, the theoretical risk of disease transmission and the existence of more economical alternatives of rationalize, we would like to emphasize the appropriate use of HSA in obstetrics and gynecology practice by the help of hospital's data, which is a tertiary care center in Turkey for Obsterics and gynecology practice. Material and Method: Retrospectively we investigate the percentage of human albumin use in term of sub departments such as perinatology, gynecological oncology and reproductive endocrinology. At the end of 2012 Ministry of health published a guideline for hospital to regulate the use of Human Albumin in medical practice. They mentioned the appropriate indications and alternative treatment methods for human Albumin use for the clinicians. The change in the HSA use indications and rate of HSA use per cases was statistically compared. Results: In 2012 Albumin use per birth in perinatology clinic is 0, 0027/birth, in 2013 it is dropped to 0, 0018/ birth. The only department that HSA use increases after implementation of guideline is gynecologic oncology Discussion: There is a significant decrease in HSA use in clinics except gynecologic oncology in daily practice. Besides this decrease inappropriate use is still common. We believe that understanding the appropriate indications and common mistakes in daily practice could be useful for gynecologists to determine the definitive treatment of options in their services.

Keywords

Human Serum Albumin; Obstetrics and Gynecology; Hypoalbuminemia; HSA

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Introduction

Human serum albumin [HSA] is the most abundant circulating protein in the body a nd show typical blood concentration of 3,5-5.0 gr/dl (35-50gr/l) [1]. It is a soluble and monomeric protein produced in the liver with a production rate of 0.2 gr/kg per day [2]. HSA synthesis is governed by a single copy gene lying on the long arm of chromosome 4, near the centromere at position q11–22 [3]. Under physiological conditions, a steady state exists between synthesis and metabolism. The amount of albumin metabolized daily is approximately 10% of total plasma albumin [4]. There is a distribution pattern of albumin that is fitted to a two-compartment model, which about 40% of albumin is stored in intravascular and 60% in the extravascular space [5]. The escape rate of albumin from intravascular space to extravascular space is increased in a variety of diseases as hypertension, major surgery and trauma, sepsis, burns etc [2].

The well-known function of HSA is providing oncotic pressure in the circulation. HSA is the main modulator of fluid distribution in the various compartments of the body as it accounts for about 70–80% of the plasma oncotic pressure [6]. Besides oncotic properties another function of albumin in the circulation is to act as a transporter for several endogenous (steroids, thyroxine, fatty acids, bile salts, metals) and exogenous (drugs; warfarin, antibiotics, furasemide) molecules. HSA also act as sweeper for oxygen radicals in the circulation with the help of free sulphydril group in its structure. The capacity to bind nitrous oxide (NO) prevents rapid inactivation of NO and causes prolongation of its anti-aggregant effect.

Clinical Use:

HSA as a colloid solution that is used for several conditions in daily clinical practice is prepared from pooled human plasma by alcoholic precipitation. For pathogen inactivation, albumin is pasteurize for at least 10 h at -60 degree Celcius [2].

HSA is largely used in clinical practice with several indications, but its administration is often inappropriate. Lots of guidelines for regulation of HSA use are published by several institutes and committees. Most widely used indication for HAS supplementation is correction of hypovolemia. Hypovolemia due to various reasons such as burns, trauma, and surgery can be indications for albumin usage. HSA usage in hypovolemia always controversial in the literature. First Cochrane meta-analysis was published in 1998 claims that infusion of HSA solutions in hypovolemia due to injury or surgery, burns and hypoproteinemia increased the risk of death by 6% [7]. However, in the following meta- analysis published in 2001 and 2004 claims that there is no increase in mortality whether HSA is used to treat hypovolemia, supporting the safety use of HSA in critically ill patients [8, 9]. Moreover, the Saline versus Albumin Fluid Evaluation (SAFE study) was also published in 2004 compared saline vs. 4% HSA solution for fluid resuscitation demonstrated that the 28-day mortality was similar [9]. Finally in 2011 the most recent meta-analysis was published by Cochrane Database showed no evidence of survival benefit of HSA compared to the other cheaper alternatives [10].

Prevention from post-paracentesis circulatory dysfunction (PPCD) which is defined as reduction of effective blood volume, rapid re-accumulation of ascites, dilutional hyponatremia, and increased mortality after large volume paracentesis is another indication for HSA administration [11]. Cirrhosis itself can be a cause for hypo-albuminemia because of decrease in production but also dilution of the extracellular fluid protein content, due to the plasma volume expansion consequent to renal sodium and water retention, and from the increased trans-capillary escape rate towards the extravascular space, at least in the most advanced stage of cirrhosis [12].

Spontaneous bacterial peritonitis, hepato-renal syndrome can be counted for other important indications for HSA use. HSA is defined as the first line treatment for these disorders [13]. The way of administration and indications for these life-threatening disorders are defined in several guidelines that are discussed earlier.

Clinical Use in Obstetrics and Gynecology:

Gynecology and obstetrics are an important specialty that Human Serum Albumin use is necessary for several different conditions. In assisted reproductive practice Ovarian Hyperstimulation Syndrome (OHSS) is one of the important conditions that characterized with hypoalbuminemia and intravascular fluid loss. Decreased intravascular oncotic pressure results accumulation of fluids in the extra-vascular areas such as pleura and peritoneum. In 2011 a Cochrane Review was published about HSA administration in OHSS. In the result section they concluded that there was borderline evidence of benefit with the routine use of human albumin in the prevention of OHSS but also they claimed that there was good evidence to support the use of hydroxyethyl starch in the prevention of OHSS in high risk patients [14]. The most common contraindication to the use of crystalloids was fluid restriction in daily practice about HSA usage [15]. By this point of view HSA use in OHSS is the most appropriate indication in gynecologic practice.

In perinatology unit HSA is also commonly used for correction of hypovolemia after surgical interventions and in special circumstances like preeclampsia. There are no controlled studies on volume substitution to correct hypovolemia in preeclampsia. In gynecologic oncology practice hypovolemia due to accumulation of ascites like in ovarian cancer or severe hypovolemia due to extensive surgery are the indications of HSA use.

For preventing the overuse of HSA in daily practice Turkish Government Ministry of Health implemented a guideline about indications for HSA use at the end of 2012. According to this guideline the indications for Albumin use is indicated for gynecology and obstetrics as follows:

1- In preeclampsia and eclampsia, the patients with serum albumin level >2g/dl

2-In OHSS, the patients with serum albumin level >2g/dl and ascites, pleural effusion or pulmonary edema

3- As additional therapy for patients with spontaneous bacterial peritonitis and ascites

In this study we try to investigate whether the implementation of Ministry of Health has made any change for the indications of HSA use in gynecology and obstetrics practice by using the data of the biggest Women Health Hospital in Turkey.

Material and Method

At the end of 2012 Ministry of health published a guideline for

hospital to regulate the use of Human Albumin in medical practice. They mentioned the appropriate indications and alternative treatment methods for human Albumin use for the clinicians. For determining the use of human albumin in gynecology and obstetrics practice and define whether any differences in clinical use after rational drug use policy for human albumin began to be implemented by Turkish Government Ministry of Health we investigate the record of our hospital which is the biggest tertiary care center for women's health in Turkey. Retrospectively we investigate the percentage of human albumin use in term of sub departments such as perinatology, gynecological oncology and reproductive endocrinology. By using the hospital's online patient database and patient charts the data about the indications for HSA use, total amount of HSA for a patient, total patients who had undergone any treatment in each subdivision in 2012 and 2013 was obtained. The indications for HSA use were investigated case by case to determine the use with correct indication according to guideline of Turkish Ministry of health for HSA use. The difference between HSA use before and after publication of guideline is statistically analyzed. SPSS 19.0 was used for statistical analysis. The demographic features of the study are demonstrated as total numbers, difference between two years was investigating by using student t test. A p-value of <0.05 was considered statistically significant.

Results

In perinatology practice, to determine the effect of Human albumin use policy Human Albumin used per birth is used. In 2012 Albumin use per birth in perinatology clinic is 0, 0027/birth, in 2013 it is dropped to 0, 0018/ birth. (Table 1) The difference between two consecutive years is statistically significant. The specific indications for Human albumin, is also changed after the active implementation of this guideline. (Table 2) Preeclamptic patients, who have volume deficit in the intravascular space, were used to be treated more often with Human albumin in 2012.

Table 1. Albumin use in perinatology department before and after drug use policy

		2012	2013
Perinatology	Total birth	17690 birhs (7996 C/S vs. 9694 Vaginal delivery)	17917 births (8412C/S vs. 9505 Vaginal delivery)
	Albumin use	48 patients	33 patients
	Albumin use per birth	0,0027	0,0018

p<0,05

In reproductive endocrinology department, most common use of albumin is for the treatment of Ovarian Hyperstimulation Syndrome. Taking into account the nature of the disease, strict volume restriction is mandatory for the treatment. If so, human albumin use is seemed to be the first choice for replacing the intravascular oncotic pressure and fluid loss. (Table 3)

Table 2. Indications for albumin use in perinatology department

Indıcatıons for Human Albumin	2012	2013
Preeclamsia	27	11
Placenta previa	7	9
Hypertension	3	2
Ablatio Placenta	2	4
DIC	2	4
Cholestasis	0	2
Not-specified	7	0

Table 3. Albumin use in reproductive endocrinology department before and after drug use policy

		2012	2013
Reproductive Endocrinology	Total Embryo transfers	362	412
	OHSS	18	9
	Albumin Use	12 patients	5 patients
	Albumin use per OHSS	0,66	0,55

p>0,05

The only department that HSA use increases after implementation of guideline is gynecologic oncology. When the indications of HSA use was investigated in more than %90 percent cases hypoalbuminemia is the cause of administration. (Table 4) In 34 out of 36 patients in 2013 was administered due to serum albumin levels below 2 g/dl. Other two patients HSA were used for supportive treatment in bacterial peritonitis and ascites.

Table 4. Albumin use in gynecologic oncology department before and after drug use policy

		2012	2013
Oncology	Total Malignant Cases	272	324
	Albumin Use	22 patients	36 patients
	Albumin use per malignant cases	0.08	0,11

Discussion

Beside the high proportion of inappropriate use, the elevated cost, the theoretical risk of disease transmission and the existence of more economical alternatives of rationalize and render more appropriate the use of HSA [16]. HSA can be prescribed as the first choice to expand effective intravascular volume in patients with advanced cirrhosis and should be used to prevent renal failure after spontaneous bacterial peritonitis and the post-paracentesis circulatory dysfunction after large volume paracentesis or to diagnose and treat hepato-renal syndrome. HSA is also the second-line treatment for fluid resuscitation in critically ill patients when crystalloids and non-proteic colloids are not effective or contra-indicated. Most common contraindication for crystalloids can be defined as fluid restriction and electrolyte imbalance. Among the heterogeneous population of ICU patients, accumulating data indicate that those with sepsis, severe sepsis, and septic shock benefit more from HSA administration.

For gynecologist OHSS is seemed to be the one of the most common condition that albumin use can be evaluated as the first line choice to replace the intravascular oncotic pressure. Ovaian carcinoma with massive ascites can be defined as other appropriate indication for HSA use. Paracentesis or surgical removal of massive ascites can cause PPCD. HSA can prevent development of PPCD. In other circumstances like preeclampsia and treatment of hypoalbuminemia after surgical interventions can be defined as inappropriate use of HSA.

Practioner tends to treat the intravascular volume deficit in pre-

eclamsia by non-coloid solutions just as crystalloids etc. after the implementation of the guideline.

The albumin use percentage in reproductive endocrinology is seemed to be remaining stable after the implementation of drug policy regimen. This can be because of the nature of hyperstimulation of ovaries, which can be defined as the only indication for albumin use in reproductive endocrinology practice, which is explained above.

The implementation of human albumin use policy does not seem to be effective for gynecologic oncology department. On contrary, the use of albumin increases between consecutive years. However, when the indications for use are investigated, this increase cannot be explained by inappropriate use. It can be explained by severity of disease and increase in total number of patients that needs HSA treatment because of their conditions and co-morbid diseases.

HSA is a lifesaving human serum protein analog whether in appropriate indications. It can be easily observed that it is inappropriately prescribed for both adult and pediatric patients. Gynecology and obstetrics should also define specific indications and guidelines for HSA use to prevent the excessive and inappropriate use of such a valuable weapon for specific conditions. The data collected from our hospital record have revealed that there is an alteration in the human albumin use after the use of human albumin policy. These alterations are in positive or negative manner in different clinics. These findings indicate that the enactment of the policy cannot be sufficient enough to ensure the decrease in inappropriate use of human albumin. There should be more organized, department based policies should be developed. Moreover the use of human albumin indications should be documented better in order to review more efficiently in the following years.

Competing interests

The authors declare that they have no competing interests.

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