

Does the Use of Highly Purified Human Menopausal Gonadotrophin (HP-HMG) avoid Ovarian Hyperstimulation Syndrome (OHSS) in Polycystic Ovary (PCO) Patients in Assisted Reproduction (IVF/ICSI)?

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Abstract

Objective: To evaluate the role of highly purified HMG (Diclair from BBT) in preventing OHSS in polycystic ovary (PCO) patients.

Design: Prospective study from 1st Aug, 2012 until end of July, 2013 for one year.

Setting: Lamis IVF center, Misurata LIBYA.

Patient(s): During one year of study, 800 patients were treated for ICSI procedure. The 20% from these cases were diagnosed as polycystic ovary.

Main outcome measure(s): Diagnosed of polycystic ovary, Age distribution, Fixed dose of 450 lu of HP HMG from BBT/day, IVF outcome and any OHSS or admission.

Result(s): age distribution counted from 20 yrs to 44 yrs old. Their eggs and embryos Quality were very good. Pregnancy rate and presence of OHSS.

Conclusion: using highly purified HMG is safe in polycystic ovary patient and can reduce or prevent the OHSS with uneffective pregnancy outcome rate.

Keywords: Polycystic ovary; Pregnancy rate; Unovulation

Introduction

In reproductive age the Polycystic ovary syndrome (PCOS) is quite common in endocrinopathies, affecting 5-10% of women [1]. Women with PCOS is present with low ovulation, hyperandrogenism and polycystic ovary syndrome [2,3] women seek treatment for infertility due to unovulation [4]. It is a heterogeneous syndrome both in its clinical presentation and in its laboratory manifestation [5,6].

Although there is significant improvement has been seen in the pregnancy outcomes with the introduction of many stimulation protocols, the incidence of ovarian hyperstimulation syndrome (OHSS) still high. OHSS is a potentially life threatening complication associated with controlled ovarian hyperstimulation and IVF, ovarian hyperstimulation syndrome can potentially rupture, hemorrhage or undergo torsion [7,8].

The pathogenesis of OHSS is unclear. The variables closely related to OHSS are beta-sub-unit of human chorionic gonadotrophin (B-hCG), S. estradiol, number of follicles, vascular endothelial growth factor (VEGF), interleukin-6, the ovarian renin angiotensin system and prostaglandins [7,9,10]. High levels of serum estrogen is

associated with increased risk of OHSS [6]. The syndrome of OHSS has been reported in extremely low S. estrogen levels [9,10].

Cancellation of the cycle to avoid the risk of OHSS but at the expenses of losing the cycle [11] with holding the human chorionic gonadotrophin (hCG) injection, coasting and elective cryopreservation of the embryos. These are all tried to avoid the flare up of OHSS. This study is randomized for patients with all ages who request management of their infertility by ICSI. This ICSI management includes short protocol and antagonist protocol for ovulation induction. The total number of patients are 800. 400 of them were having antagonist protocol.

The other 400 were having the short protocol. We were using 450 IU/day intramuscular of highly purified human menopausal gonadotrophin (HP-HMG) "Diclair of BBT" contain FSH and LH in 50% of each to find out how effective in preventing OHSS. Diclair HP HMG 150 starting from day three of cycle for 7 days but in some cases we added 2-3 days. In short protocol decapeptyl 0.05 mg (half amp) was start on day two of the cycle by injecting subcutaneously until the day of giving Human chorionic gonadotropin. In cases of antagonist protocol we were using flexible type and we give Organolutan/Cetrotide 0.25 mg S.C on day of the leading follicles measured 15-16 mm.

Patients and Methods

Eight hundred infertile women were included in this study. These patients attending the Lamis IVF Center Misurata. One hundred and sixty of them were diagnosed as Polycystic ovary syndrome based on European Society for Human Reproduction and Embryology (ESHRE)/ American Society for Reproductive Medicine guideline (Rotterdam criteria 2003), as including at least two of the following three criteria:

- 1) Chronic anovulation
- 2) Clinical or biochemical signs of hyperandrogenism
- 3) Polycystic ovary morphology shown on ultrasound scan, defined as the presence of ≥ 12 follicles (with one ovary being sufficient for diagnosis) measuring 2-9 mm in diameter.

Our inclusion Criteria were

- 1) No patient showed hyperprolactinemia, thyroid problems, liver or kidney dysfunction
- 2) All patients were for ICSI procedures
- 3) Age between 20 and 44 years. The study started from 1st august until end of July 2013 (12 months). All patients were given 450 IU of highly purified human menopausal gonadotrophin (HP-HMG) contains LH and FSH in equal form (three ampules contains 150 IU FSH and 150 IU LH in each ampule) (Table 1).

This dose was given daily intramuscular from day three of cycle until the leading follicles are measured in diameter 17-22 mm (the time of human chorionic gonadotrophin 10,000 IU to be given IM, in the same time 1/2 ampule of decapeptyl 0.1 mg was given S.C. daily, this is named short protocol. The other protocol was used in a Flexible Antagonist. Protocol (same dose of HP-HMG 450 IU/IM daily from day three of cycle until follicles are measured in diameter 15-16 mm, Antagonist 0.25 SC was given. The Human chorionic gonadotrophin 10,000 IU/IM was given after 20-24 hours of giving the antagonist (Tables 2 and 3).

Ages	20-24	25-29	30-34	35-39	40-44
Number of patients	36	174	196	236	140
Short protocol	14	84	96	126	80
Antagonist protocol	22	96	106	116	60

Table 1: Age Distribution

One egg	2-5 eggs	6-10 eggs	11-15 eggs	16-20 eggs	21-25 eggs	>25 eggs	Bad eggs
40 patients	200 patients	264 patients	160 patients	60 patients	30 patients	26 patients	20 patients
5%	25%	31.76%	20%	7.50%	3.75%	3.24%	2.50%
There were 20 patients have no eggs							

Table 2: Number of Eggs were collected

The number of eggs and Quality were observed. Quality of embryo and pregnancy were studied. Side effects and any symptoms of hyperstimulation syndrome were followed up (Table 4).

Total number of eggs	Good quality eggs which were injected by sperms	Eggs were collected very poor and were not injected by sperm
5,248	4548	700
	86.66%	13.34%

Table 3: Eggs injected with sperm and without sperm

Total Embryos	Poor Quality Embryo G3 and G4	Excellent Embryo G1 and G2
1982	392	1,590
	19.78% of total embryo	80.22% of total embryo

Table 4: Embryo Quality

Result

We had 20 patients with poor eggs and there were no fertilization. The total number of patients who had no embryo transfer were 50 patients equal to 10%. In the other hand 90% of our patients in this study were having embryo transfer. Our pregnancy rate was 45% and the early abortion was 6%. These results were almost the same in both protocol. In these eight hundred patients there were no single admissions due to hyperstimulation syndrome and there were no patients got any treatment against hyperstimulation syndrome.

The total number of patient who have polycystic ovarian syndrome in Lamis IVF Center during these twelve [12] months study were one hundred and sixty patients which is equal to 20% of total patient were treated in this time by ICSI and ET procedures (Table 5).

20-24 years	25-29 years	30-34 years	35-39 years	40-44 years
6 patients	45 patients	70 patients	35 patients	4 patients
Most of patients with polycystic ovary were at age 25-34 73%				

Table 5: Age distribution of polycystic

Discussion

The patients with ovarian hyperstimulation syndrome (OHSS) remain a challenge to manage. The ideal and successful management of high responders especially in polycystic ovary syndrome, would use as a treatment that minimizes the patient's risk while achieving optimal cycle outcome. The main advantage of using highly purified human gonadotrophin (diclair from BBT) 150 IU is the prevention of OHSS without the need to cancel the cycle. In this study more advantage were seen more than prevention of OHSS and continuation of all cycles in a form of High pregnancy rate about 45%.

Coasting 4 or more days reduces the implantation and pregnancy rate. Chen et al. [12] demonstrated increased in cancellation rates when coasting was longer more than 4 days. In our study using diclair highly purified HMG has no cycle cancellation and has good embryo implantation and pregnancy rate.

The incidence of OHSS is 20-30% for mild, 3-6% for moderate and 1-2% for severe OHSS [13,14]. According to our results OHSS has 0%. To manage severe OHSS requires ICU admission and intensive treatment. Newer management suggest treatment with cabergoline to decrease hemoconcentration and ascites by blocking the vascular endothelial growth factor (VEGF-2) receptor [15,16]. Cycle cancellation can eliminate the risk for developing OHSS completely [8,11], but the coast is not eliminated. Patient psychology will be affected from cancellation of cycle.

In this study there was no cancellation needed and no ICU management was required to a single patient, so using highly purified HMG can be the alternative and ideal drug for ovulation induction in high risk patient.

In this study the number and quality of eggs were good or not affected, while in coasted cycles the number and quality of eggs retrieved were reduced [17].

Conclusion

In conclusion, this study revealed that using Highly Purified HMG 450 Iu/Im (diclair from BBT) can save patients with polycystic ovaries from severe OHSS and in the same time give good pregnancy outcome with no cycle cancellation or holding of giving HCG.

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