

Four Years Review of Incidence and Management of Ovarian Hyperstimulation Syndrome in a Specialized Centre for Reproductive Medicine in Pakistan

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The clinical entity of ovarian hyperstimulation syndrome is a serious life threatening condition following the use of exogenous gonadotrophins for ovarian stimulation. Our objective is to find out the incidence of OHSS its clinical presentation and the most suitable treatment option for a particular situation. 679 cycles were treated by gonadotrophins in the last four years for the treatment of infertility. Twenty percent cases resulted in mild to moderate OHSS & 0.9% severe OHSS and two patients become pregnant. Out of six patients of severe OHSS two were treated conservatively and four surgically. Surgical option in the form of aspiration of fluid from the extra vascular compartments and ovarian follicles should be considered as it showed dramatic improvement.

Key words: Exogenous gonadotrophins, IVF, ICSI, OHSS

Induction of ovulation by gonadotrophins is one of the major advances in the treatment of infertility in the second half of the 20th century. Some degree of ovarian hyperstimulation occurs in all women who respond to ovulation induction but this should be distinguished from the clinical entity of ovarian hyperstimulation syndrome (OHSS). The clinical indications for exogenous gonadotrophins are rapidly increasing and they are used empirically in the treatment of luteal phase defects¹. There has been no unanimity in classifying OHSS and divergent classifications have made comparisons between the studies difficult. Raban et al² proposed the first classification of OHSS. Schenker & Weinstein later reorganized this into three main clinical categories and six grades according to the severity of symptoms and signs and laboratory. Severe OHSS is characterized by massive ovarian enlargement, ascites, pleural effusion, oliguria, haemoconcentration and thromboembolic phenomenon, is a life threatening complication^{3,4,5}.

Mild OHSS usually resolves within 2 weeks, the treatment is usually conservative with observation and follows up. On the other hand severe OHSS requires hospital admission and active monitoring. There is a sudden increase of vascular permeability, which results in the development of a massive extravascular exudate.

The aim of this study is to review the incidence of OHSS & management procedures and their outcome when gonadotrophins are used in assisted reproductive techniques. There is no published data from any ART centre of Pakistan so far, on this subject. In the international literature there is no consensus over the management of OHSS⁶.

Materials and methods

All cases who received gonadotrophins for controlled ovarian stimulation and developed OHSS were included in

the study between April 1998 to April 2002 at the Infertility Advisory Services Lahore.

IVF/ICS Protocol

Down regulation was started on 21st day of the menstrual cycle by injection of Decapeptyl 0.1mg s/c for two weeks and then gonadotrophins were started in the form of Humegon 75 or Puregon 50 (Organon, Holland) in the dose which ranges between 1-4 ampoules daily and monitoring by transvaginal ultrasound. If at least three follicles reached ≥ 18 mm, HCG injection was given in the dose ranged between 5000 to 10000 units and ovum pick up was performed 35 hours later. Luteal support was given by cyclogest 400mg daily after Embryo Transfer.

IUI Protocol

Patients who received only clomiphene citrate for induction of ovulation were not included in the study. Down regulation was not carried out in IUI (Intra Uterine Insemination). Gonadotrophins in the form of Humegon or Puregon 50 was started in early follicular phase (third or fourth day of the menstrual cycle) with or without clomiphene citrate, the starting dose was 1-2 ampoules daily and follicular tracking was done by transvaginal ultrasound. HCG injection was given in the dose of 5000 units (Pregnyl, Organon) when at least one follicle reaches ≥ 17 mm and IUI was performed for two days in that particular cycle.

Management

If OHSS occurred then each was classified according to the following classification proposed by Golan et al⁷.

Mild OHSS:

Grade 1: abdominal distension & discomfort

Grade 2: Features of grade 1 plus nausea, vomiting and /or diarrhoea; ovaries are enlarged 5-12cm.

Moderate OHSS:

Grade 3 : Features of mild OHSS plus ascites (by USG)

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Severe OHSS

Grade 4: Features of moderate OHSS plus clinical evidence of ascites and / or hydrothorax and breathing difficulties.

Grade 5: All the above plus changes in the blood volume, increased blood viscosity due to haemoconcentration, conglutination abnormality and diminished renal perfusion and function. The management carried out in all the five grades were recorded and their outcome noted down.

In all cases of severe OHSS strict chart urea and electrolytes, clotting parameters, liver function test were carried out and management was based on correction of circulatory and electrolytes imbalance. Anticoagulants if clinical or laboratory evidence of thromboembolism. Surgical management was carried out in form of aspiration of the fluid from extra vascular compartments.

Results

Total number of cases who received exogenous gonadotrophins in the last four years for IUI, IVF & ICSI

were 679 (treatment cycles). 20% of these cases developed mild to moderate degree of OHSS and 0.9% (6 cases) developed severe OHSS.

OHSS				20% (Mild to moderate)
Grade 1	95	cases		
Grade 2	23	cases		
Grade 3	18	cases		
OHSS				0.9% (Severe)
Grade 4	3	cases		
Grade 5	3	cases		

Since severe OHSS is a serious life threatening condition so we are discussing all six cases who fall in this group. Table 1 & 2 shows the details of these six cases.

Table 1 Individual details of all six cases of severe OHSS

Case No	Age	Initial Scan	ART	HMG/FSH	No. Of Follicles	HCG	L.S	Preg
1	34	PCO	ICSI	Down Reg 41 ampoules	23	6500	Cyclogest	+ Twin
2	29	PCO	ICSI	Down Reg 45 ampoules	19	6500	Cyclogest	-
3	35	Normal	IVF	Down Reg 51 ampoules	16	10000	Cyclogest	-
4	30	PCO	ICSI	Down Reg 52 ampoules	24	6500	Cyclogest	+
5	33	Mild PCO	ICSI	Down Reg 55 ampoules	18	6500	Cyclogest	-
6	28	Normal	IUI	28 ampoules	11	5000	HCG	-

Table 2: Individual details of all six cases of severe OHSS showing management and outcome

No	Clinical Picture	Management	Recovery	Hospt Stay	Outcome
1	Ascites Hydrothorax Mild breathless	Conservative Albumin infusion	Satisfactory	15 days	Recovered
2	Ascites Hydrothorax Moderate breathless	Albumin infusion	Satisfactory	12 days	Recovered
3	Ascites Hydrothorax Resp-distress	Paracentesis Follicular Aspiration	Respiratory distress markedly improved	8 days	Recovered
4	Ascites Hydrothorax Resp-Distress	Paracentesis Follicular aspiration	Respiratory distress markedly improved	9 days	Recovered
5	Moderate Ascites Leg thrombosis	Hamiplegia Heparin	Hemiplegia Recovered	16 days	Recovered
6	Ascites Hydrothorax Massive oedema & swelling vulva	Paracentesis Follicular Aspiration Albumin	Marked Improvement	14 days	Recovered

Table 3 Literature data concerning ovarian hyperstimulation syndrome (OHSS) and the protocol human menopausal gonadotrophin therapy.

Reference	Study group	Incidence of OHSS (%)	Dose	% OHSS Pregnant	HMG Regimen	Luteal support
Smits et al ¹³	1673 cycles	0.6 (severe)	Not mentioned	70	Started with 2 ampoules and adjusted to E 2	HCG 1500 iu every 72 h or cyclogest
Rizk et al ¹⁴	1562 cycles	1.3 (severe)	Not mentioned	57	Started with 2 ampoules and adjusted to E2	Hcg 2000i.u on day 2 and cyclogest
Our study	679	0.9 (severe)	28-52 ampoules	33%	Started with 2 ampoules and adjusted by TVS	HCG 5000 to 10000 iu and cyclogest

Discussion

Prevalence: Most methods of ovarian stimulation cause OHSS. Mild forms may even result from the use of oral antiestrogens.

In our series severe OHSS occurred in 0.9% of the cases which correlates with the Western literature which ranges between 0.25-2%. Mild & moderate cases in our study occurred in 20% in western it is quoted as 4%⁸. Although it seems higher but since it resolves spontaneously without admission to the hospital, it is not of much significance.

Management

Intravascular volume should be monitored. A hematocrit of over 45% is a serious warning. In our study in all cases of severe OHSS hematocrit remained normal. Schenker & weinstein⁹ reported 9 out of 25 patients showed raised hematocrit.

Thrombophlebitis occurred in 1 out of 6 case in contrast to kaaja¹⁰. In 8% of cases aspiration of the fluid from the peritoneal cavity & follicular aspiration of the ovaries, in our patients helped a lot and dramatically improved the respiratory distress and painful distension of the abdomen.

Late complications

Ong et al¹¹ reported internal jugular vein thrombosis occurring >6 weeks after ovulation and Mills et al¹² reported subclavian vein thrombosis 7 week after egg collection. Luckily in our patients nobody reported to us for delayed complication. In only one patient hemiplegia occurred who improved after couple of months.

Conclusion

1. Mild to moderate OHSS usually resolves within two weeks.
2. Severe OHSS requires hospitalization and active monitoring. There is massive increase of vascular permeability.
3. Incidence of severe OHSS is 0.9% which requires prevention or cancellation of the cycle.
4. OHSS is more common if the base line TVS show PCO like picture

5. Some time normal looking ovary can give hyper response to fertility drugs.
6. Aspiration of the ascitic fluid and follicular aspiration gives dramatic improvement in respiratory distress and painful abdominal distension.

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