
بسم الله الرحمن الرحيم

قالوا سبحانك

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سورة البقرة - الآية ٣٢

Ovarian Hyperstimulation Syndrome

Presented by

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Definition:

It is a syndrome characterized by:

variable degree of ovarian enlargement and/or ascites, pleural effusion, oliguria, hemoconcentration, thromboemolism, and electrolyte disturbances which may be life threatening.

* It occurs :

-Commonly as an iatrogenic complication of ovulation induction. -
Rarely may complicate normal pregnancy.

***Incidence:** -Mild OHSS; 8 – 23%.

- Severe OHSS: 3.5-8%

Risk factors:

- 1)**(1)Patient characters:** OHSS common with: a- Younger cases.

b- Cases with lower body weight.

c- Anovulatory cases with menstrual disorders, normal endogenous GnH, and estrogen.

d- Previous history of OHSS.

2) PCO: about 50% of OHSS cases have PCO, only 6% of severe degree.

3) Ovarian stimulation drugs:

a)GnRH:

i- **GnRH/hMG protocol**: increase the incidence of OHSS from 0.6% to up to 6.6%of moderate and severe grades. Tins may be due to:

- A direct effect of GnRH on the ovary.

- Prevention of premature luteinization allows many follicles to grow to a considerable size.

- The increased pregnancy rate and rate of multiple pregnancy.
- Increased exogenous GnH.

- The "flare up" effect of GnRH on GnH.

ii- **Pulsatile use of GnRH**: associated with mild OHSS.

3) Ovarian stimulation drugs:

b) Human menopausal gonadotrophin: OHSS is reported in up to 23% of cases (FSH+LH).

c) Pure FSH: OHSS is reported to be lower in these cases.

d) Clomid: mild degree occur in 13.5%. the incidence is increased when combined with hMG.

Risk factors:

4) Method of administration of hMG/hCG:

It was suggested that fixed schedule is associated with higher rate of OHSS.

5) Luteal phase support:

risk increased with HCG and decreased with progesterone.

6) Conception cycles:

3-4 times more risk for OHSS (longer course and severer in grade)

Pathogenesis:

The initial pathophysiological event in severe cases is increased capillary permeability specially from the enlarged ovaries leading to extravasation of fluid into the abdominal cavity causing:

1-Asctes.

2-Hemoconcentration.

3-Hypotension.

4-Decreased renal perfusion which leads to sodium and water retentions.

N.B: Renal failure may occur in the final stage due to sever volume depletion.

The suggested mediators for increased capillary permeability are:

1)Estrogen:

2) Prostaglandins:

3) Histamine

4) Prolactin:

5) Renin-angiotensin:

6) Cytokines:

7) Vascular endothelial growth factor (VEGF):

Pathogenesis:

N.B: It was suggested that haemodynamic changes are due to:

peripheral arteriolar dilatation leading to hypotension, tachycardia, and renal hypoperfusion.

However this hypothesis did not explain hemoconcentrstion commonly found in sever OHSS.

Benefits of mild OHSS:

1- Allow stimulation of more synchronous follicles.

2- Multiple mature oocytes can be fertilized.

3- Proper endometrial development - support implantation.

4- Low cycle cancellation

Recent classification of OHSS

(Jenkins&Mathur,1998)

1)Mild.

2)Moderate.

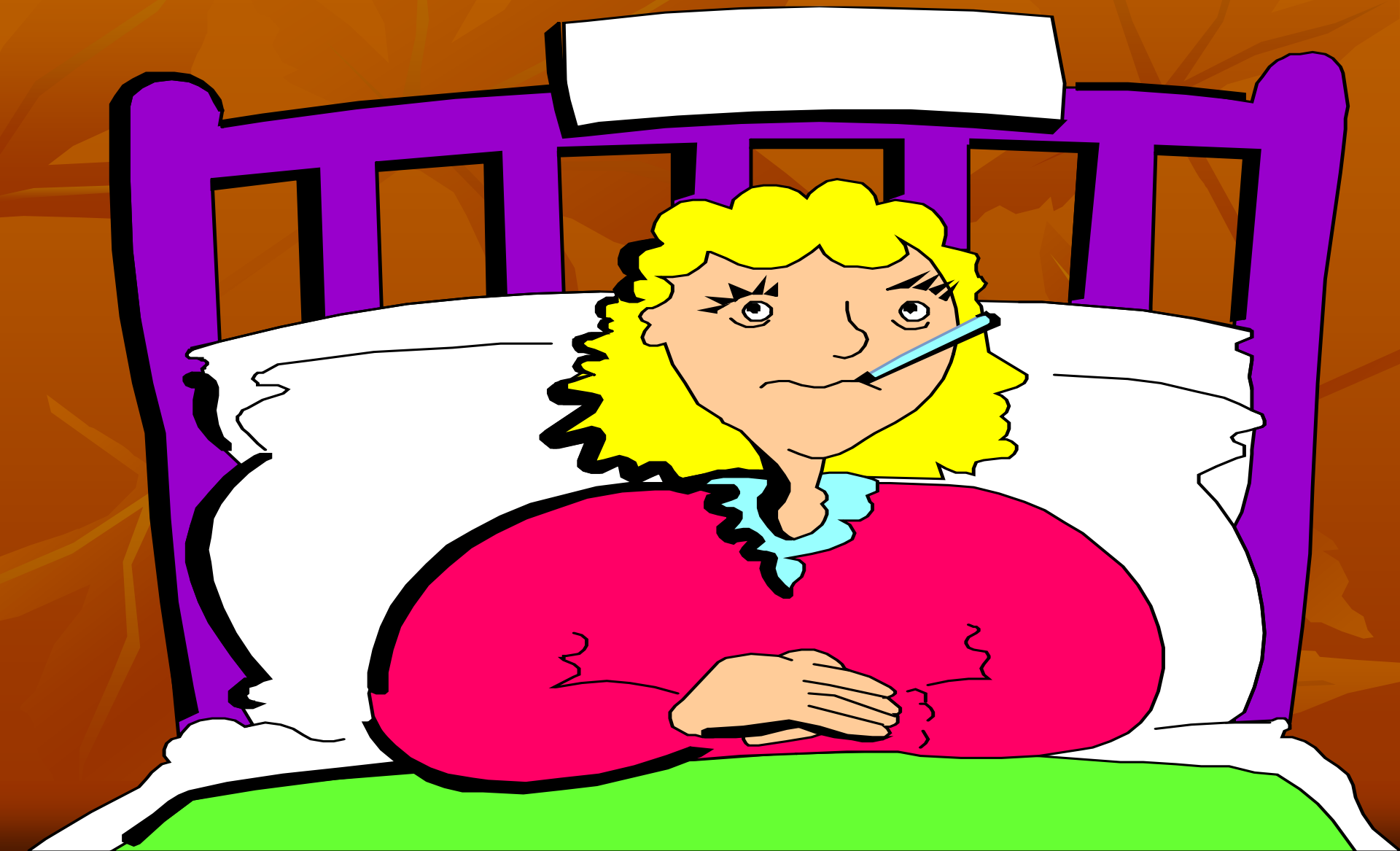
3)Severe.

4)Critical.

Grade	Ovary	Clinical	Lab. Blood
1)Mild	5- I0cc	-Abdominal Distension -GIT upset	-HCV < 45 - TLC < 15.000/cc -Normal renal function
2) *Moderate*	10-12 cc	-Moderate ascites -Body wt T 2 kg/c'ay	-HCV < 45 - TLC < 15.000/cc -Normal renal function

Grade	Ovary	Clinical	Lab. Blood
3)Sever	> 12cc	-Marked ascites -Dyspnea -Hypovolemia -Mild Thromboembolism	-HCV > 45 - TLC > 15.999/cc -Impaired renal function -
4) *Critical*	MARKED	-Tense ascites, -Hydrothorax. -Sever Thrombocmbolism. -Adult respiratory distress syndrome - **Life threatening**	-HCV(55%), -TLC > 25000/mm3, -serum creatinine> 1.6 mg%^, -creatinine clearance < 50ml/min.

Complications of OHSS:



Complications of OHSS:

1-Thromboembolic complications.

2-Liver dysfunction: liver enzymes are elevated in 15% and persist for 2 months after.

3-Respiratory complications: (adult respiratory distress syndrome).

4-Renal complications: renal failure due to hypoperfusion.

.

Complications of OHSS:

5-Adnexal torsion: due to enlargement, however laparoscopic unwinding is successful.

6-Internal hemorrhage.

7-Abortion rate: Increased form 30% to 50% in OHSS stimulated cycles after matching the maternal age.

Complications of OHSS:

8-Congenital malformation: Increased incidence due to abnormal steroid levels, abnormal body homeostasis and drugs used in treating the case , however there is increasing evidence reporting no association.

9- OHSS and ovarian cancer: The relation was suggested by some authors but with no general acceptance

Prevention of OHSS:

(Most important line of treatment).

(1)PREDICTION OF OHSS:

I) **Presence of risk factors**.

II) **Endocrine monitoring:**

A) plasma E2 level:

No risk: E2< l000 pg/ml,

High risk: E2 > 3000 pg/ml, hCG should never be given.

2 pitfalls:

1 - Cases within severe OHSS are seen with E2 levels < 1500 pg/ml.

2- Small fraction of cases will be with excessive E2.

so, slope of rise of E2 is more accurate

(considered if the value is doubled).

II) Endocrine monitoring:

B) Urinary E3 glucuronyl > 200 ug/24hrs are dangerous,

Disadvantages:

1- Retrospective (take 24h).

2- Affected by body weight.

3- Difficulties and errors in urine collection.

N.B: Recently VEGF is suggested as a predictor for OHSS.

(1)PREDICTION OF OHSS:

III) Follicular monitoring by U/S:

*It was suggested that the number of the immature follicles is more important than the number of mature follicles in predicting OHSS.

*No risk when immature follicles are < 15.

IV) Color Doppler: under trial.

(1)PREDICTION OF OHSS:

Conclusions:

It is concluded that combined E2 plasma level ± slope of rise + U/S folliculometry are accurate combination for:

-Predicting OHSS and in,

-Determining the optimum time and safety for giving hCG.

(2) Modified Stimulation Protocols:

A) Modification of HMG administration:

1- HMG Coasting: withhold hMG and continued GnRHa in cases with E2 levels > 6000 pg/ml till it reaches < 3000 pg/ml then 10000 IU of HCG was administered.

2- Titration of HMG or FHS dose in cases with PCOS: after GnRh desensitization start GnH with one ampoule to be increased by 1/2 ampoule. The total duration of stimulation is 25 day (+14 days of GnRHa) and the docs needed is about 40 ampoules.

(2) Modified Stimulation Protocols:

B) GnRh analogue:

1- Using GnRH agonist {Treptorelien 0.2 IU}to trigger ovulation instead of hCG: the drug can be used to trigger endogenous LH **(flare up effect)** to effect ovulation in cases with high risk for development of OHSS.

N.B: This method cannot be used in cycles where pituitary desensitization was performed with continuous GnP.Ha.

2-Using GnRH agonist pump.

3- Using GnRH antagonists: delay LH surge 6-7 days.

(2) Modified Stimulation Protocols:

C) Modification of HCG administration:

1- Withhold HCG administration: Don't completely prevent OHSS as endogenous LH is also involved.

2- Lower HCG doses (2000 1U).

3- Delaying HCG administration: studies are deficient and of nonconstant results.

D) Luteal phase support: use of progesterone, no HCG.

(3) Modified techniques:

1- *Follicular aspiration*: it was suggested that aspiration of the follicles is protective against OHSS since. However, Aboulghar et al (1992) found no protective effect of such method.

2- *Cryopreservation* of embryo with subsequent replacement in non stimulated or natural cycle.

3- *Selective oocyte retrieva*l in spontaneous conception cycles: This is done by puncturing most of the ovarian follicles 35 hrs after hCG administration as in IVF programs, prevent OHSS as well as multiple pregnancy.

4) Adjuvant:

1 - *Intravenous albumin administration*; why?:

a) Albumin can sequestrate any vasoactive substance released from corpora lutea or produced in the course of the disease (1/2 life of albumin =10-15 day).

b) Due to its oncotic power, it serves to maintain intravascular volume and prevent ascites, hypovolemia and hemoconcentration.

2-Hydroxyethyl-starch: Large molecule, long 1/2 life.

3- Immunoglobulin:

IgG, IgA gammglobuins have low level in patient with severe OHSS. When given IV reduce the severity.

4 - Corticosteroids:

Management of OHSS

HOW???

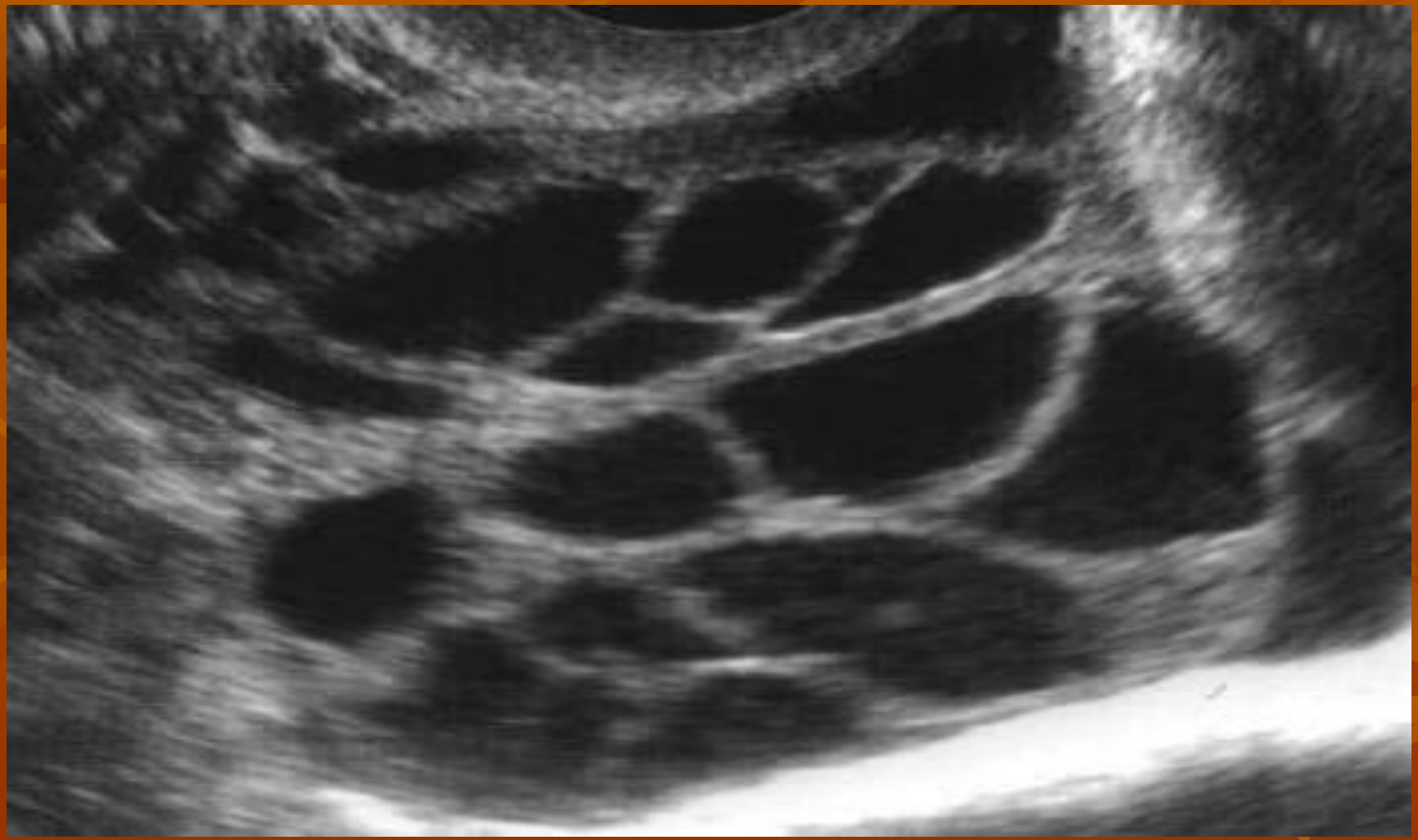
*DIAGNOSIS:

a) *History taking.*

b) Examination: (local, chest, abdomen, and for TE).

c) Investigations.

U/S for diagnosis of ovarian Hyperstimulation Syndrome



*Treatment

A- Mild cases: Spontaneous recovery within 2-3 Wk (conservative measures and follow up)

B- Moderate and severe cases:

1-General treatment:

a- Hospitalization and reassurance.

b- Observations; (ICU)

Table 2. Inpatient monitoring of patients with OHSS

Assessment	Measurements
History and Examination	Pain
	Breathlessness
	Hydration
	Weight
	Cardiovascular
	Heart rate, blood pressure
	Abdominal girth, distension, ascites
	Intake and output chart
Investigations	Full blood count
	Haemoglobin, haematocrit, white cell count
	Urea & electrolytes
	Liver function tests
	Baseline clotting studies
	Pelvic ultrasound (for ascites and ovarian size)
	Chest X-ray or ultrasonography (if respiratory symptoms)
	ECG and echocardiogram (if suspect pericardial effusion)

2- Medical treatment:

a- Circulation and electrolytes:

- Preserve the intravascular volume and renal perfusion.
- Done using colloid plasma expanders or human albumin, (effect is temporary)
- Sodium and water restriction (non effective).

b-Symptomatic treatment:

-Analgesia: paracetamol and opoids.

-Antiemetics: metoclopramid.

2- Medical treatment:

c-Prevent TE through:

- *Anticoagulant therapy:* only with:
  - Clinical evidence of thromboembolic complications.
  - Laboratory Evidence :hypercoagulability.
- *Mechanical methods.*

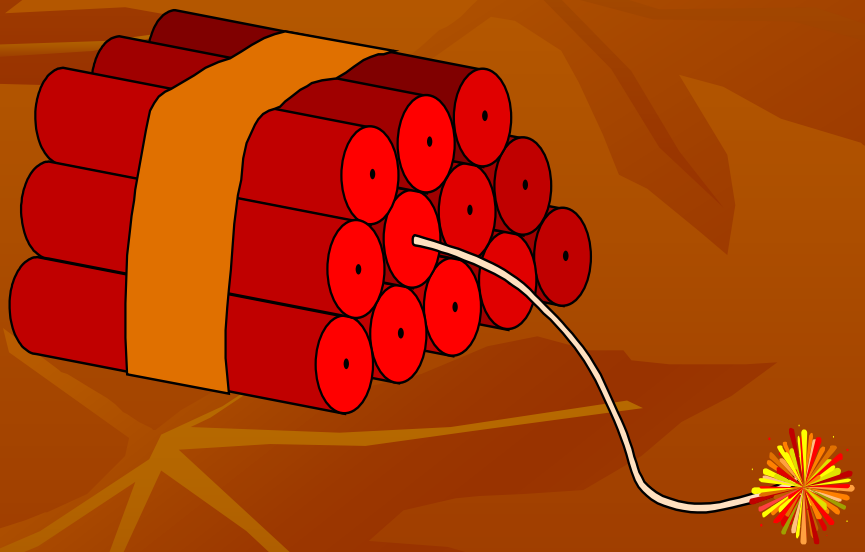
2- Medical treatment:

d- Antihistamines: was suggested to cause stabilization of capillary membrane.

e- Dopamine: in oliguric cases to improve perfusion and avoid renal failure.

f- Methotrexate: treatment of associated ectopic pregnancy to avoid surgery.

AVOID:



1- Anti-PG: disturb renal function.

2- Danazol: ineffective.

3- Diuretics: used only in pulmonary edema.

NEVER to use **Diuretics** before proper intravascular volume replacement to avoid further renal hypoperfusion

3) Aspiration of ascetic fluid or pleural effusion:

***Method:**

-Paracentesis or transvaginal aspiration under U/S guidance.

-The amount of aspirate ranges from 200-1400 ml/session.

***Advantages:**

- Improvement of respiration .
- Decrease abdominal discomfort..
- Increase venous return and COP.
- Increase urine output and createnine clearance reflecting improving renal functions.

3) Aspiration of ascetic fluid or pleural effusion

***Disadvantages:**

- Temporary effect: Recollection causes discomfort needs 3-5 days.
- Loss of large amounts of proteins (25-69g/L), so protein replacement should be effected.
- Injury of the enlarged ovaries (avoided by U/S guide).
- Introduction of infection (so use strict aseptic conditions).

4)Surgical treatment:

* ***Indications of surgery in severe OHSS:***

a- Signs of intraperitoneal Hemorrhage and/or rupture of ovarian cyst.

b- Adnexal torsion.

c- Associated ectopic pregnancy.

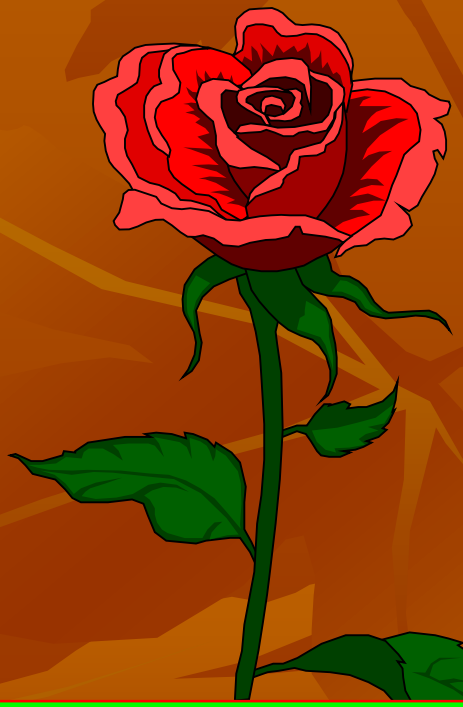
Types of surgery:

a- Laparoscopy: the ideal surgical method through which all procedures can be done.

b- Laparotomy: should always be avoided and if deemed necessary, measures are done to preserve (

ovary)

Thank you



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