

# المنتجا المترا الليتعني المنظ على المنطبط المنطلط المنطبط المنطبط المنطبط المنطبط المنطبط المنطبط المنطبط المنط المنطبط المنطبط المنط المنط المنطبط المنط المنطبط المنطبط المنط المنط المنط المنط المنطبط المنط ال



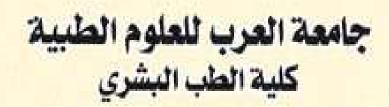




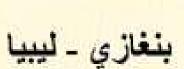








ملتقى مصراته الرابع لتشخيص وعلاج العقم



التمور/ 2008



Cyclogest









## Third Misurata Scientific meeting in the management of infertility problems Misurata / Libya



ملتقى مصراتة العلمي الثالث لتشخيص وعلاج العقم

كلية الطب البشري الجمعة:2007/10/26 MEFS Symposium Friday : 26 Oct.07

In cooperation whit MEFS and faculty of medicine - Misurata University. This symposium organized by Misurata IVF centre

Prof.M.S.Elmahaishi Ass.Prof.Omar Elsraiti Ass.Prof.M.A.Danfour Ass.Prof.Hussain M.Asherkaci Speakers

Prof.Klaus Diedrich Prof.B.C.Fauser

Dr.M.Abu-Abdalla

Dr. Hans Ingolf Nielsen

### E-mails:-

Tel:+218512620670

Fax: +218512616626

Elmahaishi@elmahaishi.com Lamis01@hotmail.com Oelsraiti@yahoo.com Mdanfour@doctor.com













# TREATMENT & PREVENTION OF OVARIAN HYPERSTIMULATION SYNDROME (OHSS) USING A DOPAMINE AGONIST CABERGOLINE (DOSTINEX)

Prof. Dr. Mohamed S. Elmahaishi

# Ovarian Hyperstimulation Syndrome

Ovarian hyperstimulation syndrome (OHSS) can occur when drugs are used to stimulate the ovaries to produce the eggs needed for fertilization in A.R.T (IVF) treatment.

# Three grades of OHSS can be diagnosed clinically and sonographicaly:

1- Mild OHSS: is associated with mild abdominal discomfort, and the ovaries are usually less than 5 cm in diameter on sonographic examination.

2- moderate OHSS: the ovaries measure between 5 and 10 cm& associated with more abdominal pain

3- severe OHSS: the ovaries are greater than 10 cm in diameter & characterized by the presence of free intraperitoneal fluid (ascites) due to increased vascular permeability.

Pleural effusions, hypotension, and oliguria have also been described.

The patient also may have fluid and electrolyte disturbances and is at increased risk for torsion of the enlarged ovaries& increased risk for thrompotic problems.

Severe OHSS occurs in fewer than 2% of patients.

this can be life-threatening.

Although ovarian hyperstimulation syndrome has been known for many years, until now it has been treated empirically and the underlying causes have been poorly understood.

The existence of a vasoactive molecule released in response to hCG & high level of E2 is believed to be the main feature associated with the increased vascular permeability that occurs with development of OHSS, and vascular endothelial growth factor (VEGF) is the main candidate as the hCG mediator (Gomez et al., Endocrinology. 2002)

dopamine has been shown to cause renal vasodilatation and diuresis.

In one study, docarpamine, an oral dopamine prodrug, was administered to 27 patients with treatment-resistant OHSS.

Diuresis was increased in some women, and ascites was decreased.

(Tsunoda et al., Gynecol Endocrinol. 2003)

Dopamine agonists are primarily used for the treatment of Parkinson's disease due to their neuroprotective effects on dopaminergic neurons.

Dopamine agonists prescribed to reduce The level of prolactin (hyperprolactinaemia).

Abnormally high prolactin may cause menstrual changes in women, and impotence in men.

can also be prescribed to prevent the production of milk in

women after birth, if breast-feeding is to be prevented for medical reasons.

A "dopamine agonist" refers to any compound which competes with dopamine for binding to the dopamine D2 receptor.

dopamine agonists include, but are not limited to, (Dostinex®) wich is a long-acting ergot derivative agonist with a high affinity for D2 receptors

Side effects Of Dostinex: Hypotention. dizziness, fainting headache nausea or vomiting unusual sleepiness constipation nosebleed weakness or tiredness temporary impairment of vision breast pain hot flushes changes in behaviour such as aggression, depression, increased sex drive

# Prevention of OHSS

For prevention of OHSS in patients undergoing fertility treatment or IVF involving the administration of gonadotrophic hormones, it is expected that administration of the dopamine agonist cabergoline will prevent an increase in vascular permeability.

Without being limited to a particular mechanism, it is expected that this will occur as a result of cabergoline binding to dopamine D2 receptors, resulting in internalization of VEGF-R2, thereby preventing binding of VEGF-A to VEGF-R2 and phosphorylation of VEGF-R2.

Claudio Alvarez, from the Instituto Valenciano de Infertilidad, Valencia, Spain, said that his team's work, using the dopamine agonist Cabergoline (Dostinex), was the first successful attempt to prevent this disorder.

Animal models had shown that increased vascular permeability, a factor in ovarian hyperstimulation syndrome, was associated with an increased expression in the ovary of vascular endothelial growth factor (VEGF), responsible for the growth of blood vessels. The binding of VEGF to its receptor VEGFR2 increases vascular permeability.

" We knew that dopamine and its agonists also reverse increased vascular permeability in hyperstimulated animals", said Alvarez, "

so we decided to see whether it could prevent ovarian hyperstimulation syndrome in women undergoing ovarian stimulation for ART."

for prevention, cabergoline (Dostinex®) is administered during controlled ovarian stimulation (with gonadotropins or other ovarian stimulating agents) prior to triggering final maturation/ovulation with e.g., hCG. Preferably, administration is initiated during the last week of stimulation. Administration is continued for about one to three weeks after hCG stimulation.

For treatment of OHSS, administration of cabergoline is initiated once a patient has been diagnosed with moderate to severe OHSS(when signs and symptoms of OHSS first appear) . at a dose of about 0.05 to 1.0 mg/day from about 1 to about 28 days, preferably from about 7 to about 14 days, or until symptoms abate.

Source: European Society for Human Reproduction and Embryology, 2006).

"We found that Cabergoline reduced hemoconcentration, ascites and the incidence of moderate to severe ovarian hyperstimulation syndrome in women at risk," said Alvarez

At our clinic (Misurata IVF center & lamis IVF center) We start to use use destinox at january 2008.

we use destinox for 26 cases;

4 pt as therapeutic measure; they present with OHSS & pregnancy.

one of them present with twins pregnancy &two with triplets pregnancy &one with 5 fetuses.

In this group of pt we used dostinex one tab 0.5mg /day for 10 days.

Fetal reduction to two fetuses done for all.

One ended by abortion at 20 wks.

One of them delivered by c/s healthy boy & girle.

One now at 36wks

One at 30wks& both twins pregnancy at good general condition.

# We Use destinox as prophylactic of 0HSS for 22 cases

- The criteria for using destinox in this group were:
- 1. No of egges picked up for ICSI = 20 eggs or more.
- 2. Ovarian size from 10 15 cm tascites.

3. E2 level at day of ovum pick up >2000pg/ml

The dose of Destinox was 0.5mg tab once daily for 5days started at day of pick up.

E.T were done in blastocyst stage.

all pts were seen again at two wks post E.T for serum BhcG level & transvaginal uss.

In all pt there were no signs or symptoms of OHSS.

Ten pt out of 22 pt were pregnant.

Since using destinox we have no admitted cases with OHSS.

So now we are using it as prophylactic measure for OHSS.



# THANKS