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Egyptian Pharmaceutical Vigilance Center (EPVC)

Pharmacovigilance Department

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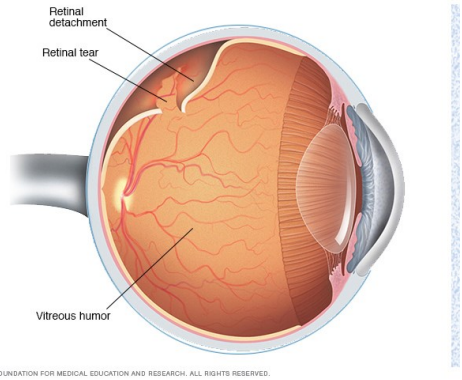
Fluoroquinolones and potential risk of retinal detachment

Oral fluoroquinolones are antibiotics used to treat bacterial infections.



A Health Canada safety review was carried out as a follow-up assessment on the potential risk of retinal detachment with the use of oral fluoroquinolones. the previous safety review examined the risk of retinal detachment with oral fluoroquinolones and had concluded that limited evidence was available to support a link at that time. Since Health Canada's initial review, many other studies have been conducted regarding the potential link between the use of oral fluoroquinolones and retinal detachment triggering this follow-up safety review.

Retinal detachment is a painless separation of the retina from the layer of support tissue and blood vessels at the back of the eye that provides the retina with oxygen and nourishment. Symptoms related to retinal detachment depend on the location and extent of the detachment, and may include the sudden appearance of debris in the field of vision (look like spots, hairs or strings and seem to float across one's vision -- floaters), the perception of flashes of light in the affected eye, the sensation that a shadow or curtain has come down over a portion of the visual field, or even sudden and complete loss of vision in the affected eye. Retinal detachment is considered a medical emergency and requires immediate attention to prevent permanent visual damage.

Plausible mechanism for retinal detachment

The exact mechanism of retinal detachment with fluoroquinolones is unknown. The retina is a delicate structure within the eye attached to the cortical vitreous by a complex matrix of collagen fibers. Vitreous liquefaction, a normal aging change of the vitreous, can result in retinal traction, which in turn can lead to retinal tears and subsequently retinal

detachment. Conditions that interfere with connective tissue and collagen formation also increase vitreous liquefaction and have been shown to increase the risk of retinal detachment. Isolated animal studies have shown that fluoroquinolones interfere with collagen synthesis 10 and disrupt the extracellular matrix outside the retina, including the corneal matrix. 11 Hence it is postulated that fluoroquinolones could damage connective tissue including that of the vitreous and vitreous cortex through the aforementioned mechanisms observed in animals, potentially leading to retinal detachment.

Conclusions:

- The link between the use of fluoroquinolones and the occurrence of retinal detachment cannot be ruled out at the present time.
- If patients experienced vision problems during or following oral fluoroquinolone administration, you should contact the Healthcare professional

References:

1. *Health Canada -Summary Safety Review - Oral FLUOROQUINOLONES (Click here)*
2. *Singapore -Fluoroquinolones and potential risk of retinal detachment (Click here)*

Case report from Sohag - Ovarian hyper stimulation syndrome (OHSS) induced by using Menogon & Purogon &Clomid as ovulation induction therapy

The Egyptian pharmaceutical Vigilance regional center in Sohag (EPVC-Sohag) has received an ICSR for an adult female patient- 30 years old who had administrated oral contraceptive pills since 2012 then she stopped these pills.

Three months later, she started ovulation induction therapy; Menogon 75mg, Puregon 100 IU /0.5 ml as intramuscular injection once on the last day of the menstruation and Clomid 50 mg oral tablets for 10 days before the menstruation and 10 days after it.

She suffered symptoms of cramps, sever pain and weight gain, so the therapy had been withdrawn, then she suffered from severe bleeding which recovered by medical intervention.

Menogon:-

1 ampoule with powder contains: Menotropin corresponding to 75 IU FSH and 75 IU LH.

Used for Sterility in females with hypo- or norm gonadotropic ovarian insufficiency, Stimulation of follicle growth and Sterility in males with hypo- or norm gonadotropic hypogonadism.

Puregon:-

PUREGON belongs to a group of medicines called "gonadotropins" It contains (FSH) in a solution in a cartridge produced by mammalian cells, by recombinant

DNA technology was changed to carry the genes for human FSH. It is very similar to the natural human FSH, which is normally secreted by a small gland at the base of the brain, the pituitary. Together with (LH), FSH controls the action of the sexual glands (ovaries in women and testes in men).

Clomid:-

Clomid (clomiphene) is a non-steroidal fertility medicine. It causes the pituitary gland to release hormones needed to stimulate ovulation (the release of an egg from the ovary).

Clomid is used to cause ovulation in women with certain medical conditions (such as polycystic ovary syndrome) that prevent naturally occurring ovulation.

Ovarian hyper stimulation syndrome (OHSS):-

Is an iatrogenic complication of assisted reproduction technology, The syndrome is characterized by cystic enlargement of the ovaries and a fluid shift from the intravascular to the third space due to increased capillary permeability and ovarian neoangiogenesis. Its occurrence is dependent on the administration of human chorionic gonadotrophin.

OHSS has been recognized in two forms: The early form of OHSS, (within days after the ovulation triggering injection of (HCG) although elicited by HCG, is related to an exaggerated ovarian response to gonadotrophin stimulation, whereas the late form (10 days after HCG)is mainly related to the secretion of placental HCG.

Upon search it was found that:

OHSS pathophysiology and etiology:-

- The physiopathology of OHSS is increasingly better understood. The crux is equilibrium between pro- antigenic and antiangiogenic factors present in follicular fluid.
- The incidence of moderate OHSS is estimated to be between 3 and 6%, while the severe form may occur in 0.1-3% of all cycles.
- The early warning signs of OHSS are abdominal pain and distention
- When signs of OHSS occur, the patient must be adequately informed and hospitalization should be proposed at the slightest deterioration, admission to an intensive care unit is necessary when critical OHSS develops.
- OHSS may progress rapidly (within 24 hours to several days) and Its impact on the general health of the patient can be very deleterious and fatal
- The ovarian hyper stimulation syndrome (OHSS) has been reported to occur in patients receiving clomiphene citrate therapy for ovulation induction.
- OHSS is extremely rare without HCG administration.
- The relationship between HCG and OHSS is thought to be mediated via the production of the angiogenic molecule VEGF (*vascular endothelial growth factor)*.

RECOMMENDATIONS:

* If gonadotrophin stimulation for ovulation induction is unavoidable, one should use "friendly" stimulation regimens aiming at (SOFT: *Suppression of Ovarian Function Trial*) single ovarian follicle viz., low-dose step-up regimen, step-down regimen, use of antagonists, and utilization of blood and sonographic control of ovarian response.
* HCG as an ovulation trigger should be

replaced by safer methods like rLH and endogenous GnRH-surge by an agonist.

* To minimize the hazard associated with occasional abnormal ovarian enlargement associated with CLOMID therapy, the lowest dose consistent with expected clinical results should be used
* To reduce the risk of OHSS, ultra-sonographic assessments of follicular development should be performed prior to treatment and at regular intervals during treatment. The concurrent determination of serum oestradiol levels may also be useful.
* Prophylactic albumin administration may interrupt the development of OHSS by increasing the plasma oncotic pressure and binding mediators of ovarian origin. This effect could be counteracted by increased capillary permeability.

References:

1. Ncbi-article-Ovarian hyperstimulation syndrome (Click here)

2. Article-The Journal of Obstetrics and Gynecology of India (Click here)

3. FDA-label-MENOTROPINS FOR INJECTION, (Click here)

4. FDA-label-clomiphene citrate (Click here)

5. SPC-Puregon (Click here)