

# **Egyptian Fertility Sterility Society**

## **The 25<sup>th</sup> Editorial**

### **Does paracetamol interfere with cell division and thereby disrupt pre-implantation embryonic development?**

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#### **What is Known Already?**

Data from the last decades have shown that an estimated 10–40% of all embryos fail to implant, and an additional 10% of pregnancies are likely lost after implantation but before clinical recognition ( [1-7]

Over-the-counter mild analgesic paracetamol (known as acetaminophen Panadol®) is the active pharmaceutical ingredient in more than 600 different medications used to relieve mild to moderate pain and reduce fever [8].

Paracetamol is widely used by women of reproductive age and during pregnancy, as it has been considered of minimal risk for use during pregnancy. [9]

The maximum single dose (oral or parenteral) 1000 mg and the maximum dose 4000 mg per 24 hours [10]

Although studies have shown that paracetamol exposure at non-cytotoxic levels inhibits cell proliferation, impairs DNA repair, and increases DNA fragmentation [11-15], up to 65% of pregnant women in the USA and an estimated 50% globally use paracetamol [16-20]. While these studies have yielded novel insights into abortion and preterm labor, they do not fully elucidate the risk of early embryonic loss within the first weeks of pregnancy.

## What is New?

A recent study done at Denmark in 14 medical department by 26 authors encompassing human embryos and mouse pregnancy model. [21]

- I. Human model: A total of 90 human embryos were exposed in vitro (22 cleavage stage and 68 blastocyst-stage embryos)
- II. Mouse pregnancy model: Experiments were run in two independent cohorts of 24 females and 12 males. Upon arrival, females were housed in 12 boxes of two and males six-by-six.

This recent study reported that after exposure to paracetamol, it is found that:

- 1-A hindered cell cycle progression, likely by inhibiting ribonucleotide reductase, leading to reduced DNA synthesis and accumulation in the S-phase.
- 2- A decreased cell numbers in mouse and human cleavage-stage embryos or caused direct embryonic death
- 3- Similar exposure to mouse and human blastocyst-stage embryos resulted in a reduced inner cell mass and decreased DNA synthesis, respectively

## Implications of This Findings:

The widely used mild analgesic paracetamol could contribute to early embryonic loss by impairing initial cell divisions. Thus paracetamol should be used with caution by women attempting to conceive (minimal dosage and duration when indicated with cold compress for hyperpyrexia or rest for pain).

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