

NSAIDs Dramatically Reduce Ovulation With Consistent Use

Pam Harrison | June 16, 2015

ROME — Nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to inhibit ovulation and reduce progesterone levels in young women, which could seriously undermine fertility, new research suggests.

"I'm actually a very late whistleblower because many others have tried to say the same thing: that NSAIDs — which are widely used and can be bought without a prescription — prevent the ovarian follicle from rupturing so women who are taking NSAIDs cannot release an ovum to be fertilized," said Sami Salman, MD, from the University of Baghdad.

Although "this process is reversible, a woman is not going to get pregnant if she continues to take NSAIDs, and doctors need to advise women to stop taking these drugs if they want to be fertile," he told *Medscape Medical News*.

Dr Salman presented the study results here at the European League Against Rheumatism Congress 2015.

He and his colleagues evaluated 39 women of childbearing age who presented to a rheumatology clinic in Baghdad with minor back pain.

The women were assigned to one of four treatment regimens: diclofenac 100 mg/day, naproxen 500 mg twice daily, etoricoxib 90 mg/day, or placebo.

Before the initiation of treatment, each woman underwent an ultrasound to assess the diameter of the dominant follicle, ovary size, and endothelial thickness.

Doctors need to advise women to stop taking these drugs if they want to be fertile.

Because progesterone, which is essential for ovulation and the implantation of a fertilized embryo, is known to be affected by NSAIDs, progesterone levels were also measured.

The treatments were initiated on day 10 of a woman's cycle to ensure a follicle was being readied for release, Dr Salman explained.

After 10 continuous days on the treatment regimen, the women underwent another ultrasound to assess the effect of the therapy.

The dominant follicle remained unruptured in 75% of women in the diclofenac group, 25% in the naproxen group, 33% in the etoricoxib group, and 0% in the placebo control group.

"All control patients on placebo ovulated, but ovulation was far less frequent in patients who were on NSAIDs," Dr Salman reported.

"For those taking diclofenac, ovulation was reduced by an amazing 93%, whereas for both naproxen and etoricoxib, ovulation was reduced by about 75%," he added. "This was really a shocking finding."

After 10 continuous days of NSAID use, there was a significant decrease in progesterone.

NSAIDs also had an effect on the dominant follicle.

Table: Effect of Treatment on Mean Dominant Follicle Diameter

Treatment Group	Before Treatment, mm	After Treatment, mm	P Value
Diclofenac	12.5	22.0	0.001
Naproxen	13.8	17.6	0.366
Etoricoxib	14.8	19.8	0.286
Placebo	12.7	0.0	—

Unruptured follicles were more common in the diclofenac group than in the naproxen group (12 vs 4).

The number of cysts was similar in the diclofenac, naproxen, and etoricoxib groups (3 vs 5 vs 6).

"This means that across all treatment groups, about one-third of patients developed a functional cyst due to the unruptured follicle," Dr Salman explained.

The investigators were able to convince about half of the women to return the next month for assessment of ovulation.

After the discontinuation of NSAIDs, all the women "did ovulate normally during the next cycle," he reported. "This convinced us that the anovulatory effects of NSAIDs are reversible."

"Nevertheless, these findings highlight the harmful effects NSAIDs may have on fertility, and they could even open the door for research into new emergency contraception with a more favorable safety profile than those currently in use," he added.

The potential negative effects of NSAIDs on fertility have been reported for many years.

The study is pertinent to rheumatologists for a number of reasons, said Philip Conaghan, MD, from the University of Leeds in the United Kingdom.

"First, it reminds us that we should be knowledgeable about uncommon side effects of drugs we use frequently," he said in written correspondence. "The potential negative effects of NSAIDs on fertility have been reported for many years."

Second, Dr Conaghan noted, although most NSAID use is in the postmenopausal age group, is intermittent, or both, rheumatologists see a substantial number of younger women — for whom fertility is often an issue — with inflammatory diseases who use NSAIDs frequently.

"This work is a timely reminder to consider the role and timing of NSAIDs in these patients," Dr Conaghan told *Medscape Medical News*.

"Another interesting aspect of the study is that diclofenac seemed to have more effect than a coxib, contrary to some reports," he pointed out.

Dr Salman and Dr Conaghan have disclosed no relevant financial relationships.

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