

Levonorgestrel emergency contraceptive pill found to be more effective when taken with an anti-inflammatory medication

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Taking piroxicam, an anti-inflammatory medication commonly used for arthritis pain, at the same time as the levonorgestrel emergency contraceptive pill after unprotected sex prevents significantly more pregnancies compared to taking levonorgestrel alone, according to a randomized controlled trial published in *The Lancet*.

Two types of emergency contraceptive pills—containing either [levonorgestrel](#) or ulipristal acetate—are the most widely used emergency [contraception](#) method in most countries, with the levonorgestrel pill available in more countries than the ulipristal acetate pill. Both contraceptives work by preventing or delaying ovulation and neither are effective post-ovulation.

The accepted effectiveness of levonorgestrel is based on the results of a trial from 1998 in which levonorgestrel prevented 95% of expected pregnancies when taken within 24 hours of [unprotected sex](#), 85% if taken within 25–48 hours, and 58% if taken within 49–72 hours. However, more recent research suggests the efficacy of levonorgestrel might be lower.

"The levonorgestrel emergency contraceptive pill is one of the most popular choices of emergency contraception in many parts of the world, so finding out that there is a widely available medication which increases levonorgestrel's efficacy when they are taken together is really exciting," said Dr. Sue Lo from the Family Planning Association of Hong Kong, a co-investigator of the study.

First author of the study Dr. Raymond Li from The University of Hong Kong added, "Our study is the first to suggest that a readily available and safe medication taken at the same time as the levonorgestrel pill can prevent more pregnancies than levonorgestrel alone. We hope these results will lead to further research and ultimately changes in clinical guidelines to enable women around the world to access more effective

emergency contraception."

The study took place at a major community sexual and reproductive health service in Hong Kong between August 2018 and August 2022. Women who required levonorgestrel emergency contraception within 72 hours of unprotected sex were randomized to receive a single supervised dose of levonorgestrel 1.5 mg plus either piroxicam 40 mg or a placebo pill.

The participants and the attending health care professionals did not know which group received which treatment. A follow up appointment was scheduled one to two weeks after the next expected period. During the appointment, if a normal period had not occurred by that time, a [pregnancy test](#) was carried out. The proportion of pregnancies prevented out of those expected was calculated based on an established model published in 1998.

Of the 836 women followed up, there was one pregnancy among the 418 women who took piroxicam and levonorgestrel and seven pregnancies among the 418 women who had the placebo and levonorgestrel. The percentage of expected pregnancies without contraception was estimated at 4.5% (19/418) in both groups. Therefore, the percentage of pregnancies prevented following piroxicam- levonorgestrel co-treatment was 95% (18/19), compared with 63% (12/19) in those who took levonorgestrel and placebo.

There were no significant differences in the rates of side effects between those receiving piroxicam and placebo co-treatment.

Professor Kristina Gemzell-Danielsson from the Karolinska Institute, another co-investigator, explained that "levonorgestrel prevents [pregnancy](#) by blocking or postponing the luteinizing hormone surge, which disrupts the ovulatory process. Piroxicam might work by targeting

a different type of hormone—prostaglandins. Prostaglandins facilitate several reproductive processes including ovulation, fertilization, and embryo implantation."

"Therefore, we speculate that piroxicam may provide a contraceptive effect both pre-ovulation (by blocking the ovulatory process) and post-ovulation (by preventing the implantation of the embryo), however our trial did not investigate piroxicam's mechanism of action and further studies are required to confirm this."

The authors acknowledge some limitations of the study, including the generalizability of the findings to other settings. As the study excluded women with current or recent use of hormonal contraception, as well as those with more than one episode of unprotected sex before taking emergency contraception, it is not certain whether the piroxicam-levonorgestrel co-treatment will be equally effective when applied to women in those circumstances.

Writing in a linked Comment, Dr. Erica Cahill from Stanford University School of Medicine, who was not involved in the study, said, "Overall, this study suggests that anyone administering levonorgestrel 1.5 mg as [emergency contraceptive pills](#) should consider the addition of 40 mg piroxicam orally, as it improves efficacy with minor side-effects."

"These conclusions might not apply to all patients, as this study was limited by a specific population, with participants being mostly of Asian ethnicity and weighing less than 70 kg. Given that levonorgestrel emergency contraception is less effective in people with obesity, the efficacy shown here might not be generalizable to patients with higher BMIs."

More information: Oral emergency contraception with levonorgestrel plus piroxicam: a randomised double-blind placebo-controlled trial, *The*

Lancet (2023). [www.thelancet.com/journals/lan ... \(98\)05145-9/fulltext](http://www.thelancet.com/journals/lan... (98)05145-9/fulltext)

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