Q2 NSAID and Emergency Contraception

Oral piroxicam 40 mg co-administered with levonorgestrel improved efficacy of emergency contraception.

- ❍ True
- ❍ False

Educational Point: Emergency contraception (EC) is used to prevent unwanted pregnancy after unprotected sexual intercourse, sexual assault, or after a recognised contraceptive failure such as a condom accident or missed dose of hormonal contraception. Availability of effective EC methods is important for reducing the occurrence of unwanted pregnancies in these circumstances. Oral hormonal EC is the most widely adopted method, both in Hong Kong and most other countries. The EC method currently available for oral use consists of a single dose of 1.5 mg levonorgestrel to be taken within 72 h of unprotected sexual intercourse, or 30 mg ulipristal acetate (UPA) to be taken within 120 h of unprotected sexual intercourse.

Levonorgestrel is effective as an EC only when given before, but not after, ovulation. This can be explained by its mechanism of action. Levonorgestrel prevents pregnancy by blocking or postponing the luteinising hormone surge, hence disrupting the ovulatory process; this effect is limited to its administration before the onset of the luteinising hormone surge, but not when it is taken after the luteinising hormone surge has started, a time when intercourse is most likely to result in pregnancy. The later in the follicular phase that levonorgestrel is taken, the lower its ability to block ovulation, and thus prevent fertilisation, will be. Once the ovulatory process has been triggered by the luteinising hormone surge, levonorgestrel cannot prevent release of an oocyte. Levonorgestrel has no effect on sperm function, fertilisation, or implantation.

Prostaglandins facilitate several reproductive processes including ovulation, fertilisation, tubal function, and embryo implantation. It is therefore possible that an inhibitor of the cyclo-oxygenase (COX) enzyme, the key enzyme involved in prostaglandin production, might act synergistically with oral EC methods to improve their efficacy in regulating both ovulatory and post-ovulatory processes.

This was a randomised double-blind placebo-controlled trial carried out in a major community sexual and reproductive health service in Hong Kong. Women who required levonorgestrel EC within 72 h of unprotected sexual intercourse were recruited and block-randomised in a 1:1 ratio to receive a single supervised dose of levonorgestrel 1.5 mg plus either piroxicam 40 mg or placebo orally. Piroxicam was chosen for this purpose as it is one of the longest-acting COX inhibitors commercially available. Group assignment was concealed in opaque envelopes and masked to the women, clinicians, and investigators. At follow-up 1–2 weeks after the next expected period, the pregnancy status was noted by history or pregnancy test. The primary efficacy outcome was the proportion of pregnancies prevented out of those expected based on an established model. All women randomised to receive the study drug and who completed the follow-up were analysed.

860 women (430 in each group) were recruited between Aug 20, 2018, and Aug 30, 2022. One (0.2%) of 418 efficacy-eligible women in the piroxicam group were pregnant, compared with seven (1.7%) of 418 in the placebo group (odds ratio 0.20 [95% CI 0.02–0.91]; p=0.036). **Levonorgestrel plus piroxicam prevented 94.7% of expected pregnancies compared with 63.4% for levonorgestrel plus placebo.** The authors noted no significant difference between the two groups in the proportion of women with advancement or delay of their next period, or in the adverse event profile.

Oral piroxicam 40 mg co-administered with levonorgestrel improved efficacy of EC in this study. Piroxicam co-administration could be considered clinically where levonorgestrel EC is the option of choice.

The correct answer is true.