



Multicentre, prospective, double-blind, randomised controlled clinical trial comparing different non-opioid analgesic combinations with morphine for postoperative analgesia: the OCTOPUS study

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BACKGROUND: Head-to-head comparisons of combinations of more than one non-opioid analgesic (NOA) with morphine alone, for postoperative analgesia, are lacking. The objective of this multicentre, randomised, double-blind controlled trial was to compare the morphine-sparing effects of different combinations of three NOAs-paracetamol (P), nefopam (N), and ketoprofen (K)-for postoperative analgesia.

METHODS: Patients from 10 hospitals were randomised to one of eight groups: control (C) received saline as placebo, P, N, K, PN, PK, NK, and PNK. Treatments were given intravenously four times a day during the first 48 h after surgery, and morphine patient-controlled analgesia was used as rescue analgesia. The outcome measures were morphine consumption, pain scores, and morphine-related side-effects evaluated 24 and 48 h after surgery.

RESULTS: Two hundred and thirty-seven patients undergoing a major surgical procedure were included between July 2013 and November 2016. Despite a failure to reach a calculated sample size, 24 h morphine consumption [median (inter-quartile range)] was significantly reduced in the PNK group [5 (1-11) mg] compared with either the C group [27 (11-42) mg; $P < 0.05$] or the N group [21 (12-29) mg; $P < 0.05$]. Results were similar 48 h after surgery. Patients experienced less pain in the PNK group compared with the C, N, and P groups. No difference was observed in the incidence of morphine-related side-effects.

CONCLUSIONS: Combining three NOAs with morphine allows a significant morphine sparing for 48 h after surgery associated with superior analgesia the first 24 h when compared with morphine alone.

CLINICAL TRIAL REGISTRATION: EudraCT: 2012-004219-30; NCT01882530.

Résumé en anglais

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