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Oral choline supplementation for postoperative pain

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Editor's key points

- There is a need for adjuvant analgesics to improve postoperative analgesia and reduce opioid consumption.
- Basic science studies have demonstrated a potential anti-inflammatory and analgesic effect of choline.
- This study examined effects of oral choline on postoperative pain and tumour necrosis factor (TNF) levels.
- Neither pain nor TNF was affected, despite a small increase in systemic levels of choline.
- While further study may be warranted, oral choline supplementation does not confer any analgesic benefit.

Background. Activation of nicotinic receptors with nicotine has been shown to reduce post-surgical pain in clinical and preclinical studies. Choline is a selective agonist at α7-type nicotinic receptors that does not have addictive or sympathetic activating properties. It is anti-nociceptive in animal studies. We conducted a double-blind randomized trial of oral choline supplementation with lecithin to aid in the treatment of pain after gynaecological surgery.

Methods. Sixty women having open gynaecological surgery were randomly assigned to receive 20 g of lecithin before surgery or placebo. Plasma choline concentration and tumour necrosis factor (TNF) were measured. Pain report was the primary outcome measure.

Results. We achieved a small but statistically significant increase in choline after surgery with oral supplementation. Plasma TNF was not decreased and pain report was not different between groups at rest or with movement. There were no adverse effects of treatment.

Conclusions. Oral supplementation with lecithin during the perioperative period resulted in very slow absorption and thus only a small increase in plasma choline was achieved. This concentration was inadequate to reduce TNF as has been shown in other studies. The absence of an anti-inflammatory effect was likely related to our failure to demonstrate efficacy in pain reduction.

Keywords: analgesia; anti-inflammatory agents; nutritional requirements; pain; pain measurement

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Seventy to eighty per cent of the 23 million Americans who undergo surgical procedures each year experience moderate-to-severe pain, despite 'state of the art' treatment.[1–3] Extended hospitalization, compromised prognosis, and higher morbidity and mortality are consequences of inadequately managed acute postoperative pain.[4] Opioid agonists are the current mainstay of pain treatment after surgery, but opioid therapy is severely limited by side-effects at effective doses. There is some evidence that the advent of patient-controlled analgesia and epidural analgesia has reduced the incidence of unacceptable pain relief,[5] but the situation is still far from perfect for many patients. For many patients, there is no dose of opioid alone that adequately treats acute postoperative pain without unacceptable side-effects. For this reason, although patients have access to large doses of opioids via patient-controlled analgesia pumps, they choose to accept moderate-to-severe pain rather than taking more opioid.[6–8]

Multimodal pain therapy combines administration of adjuvant analgesic drugs with opioids to reduce the required dose, and thus side-effects that occur when each drug is used alone. Non-specific activation of nicotinic acetylcholine receptors with nicotine has analgesic efficacy as an adjuvant for postoperative pain,[6 9–12] but its use is limited by side-effects such as nausea, autonomic dysfunction, and concerns about addiction to nicotine. Choline is a nutritional supplement that selectively activates α7 nicotinic acetylcholine receptors[13 14] and potentially α8,α9-containing nicotinic receptors[15] but not the α4β2 subtypes that are associated with nausea and addictive properties or the α3β4 subtypes

that are expressed in the autonomic nervous system. α7-containing nicotinic receptors are expressed in the central and peripheral nervous system and on immune cells where their activation reduces the production of inflammatory cytokines via a pathway that involves the transnucleation of nuclear factor kappa b and decreased production of tumour necrosis factor (TNF).[16] Systemically administered choline has been shown to have analgesic efficacy in preclinical trials potentially through a reduction in surgically induced inflammation.[17–23]

In this double-blind, randomized trial, we tested the hypotheses that oral choline supplementation can raise plasma choline concentration, mitigate the inflammatory response to surgery via the TNF pathway, and thus result in analgesia. To test this hypothesis, we enrolled 60 women who planned open gynaecological surgery into a double-blinded randomized trial of choline supplementation.

Methods

Ethical approval for this double-blind, placebo-controlled pilot study was obtained by the Institutional Review Boards at Columbia University Medical Center and The University of California, San Francisco. The trial is registered with clinical trials.gov (NCT00720343) and is conducted under investigator IND 101516 from the FDA.

Sixty women between the ages of 18 and 60 were recruited at a preoperative visit at Columbia University Medical Center who planned hysterectomy or myomectomy through a low transverse incision (Fig. 1). Chronic pain or pain medication use, tobacco use, choline or soy intolerance, active psychiatric disease, pregnancy, and lactation were exclusion criteria.

Each subject was assigned via a random allocation table maintained by the research pharmacy to receive either choline supplementation or placebo study drug (gelatin).

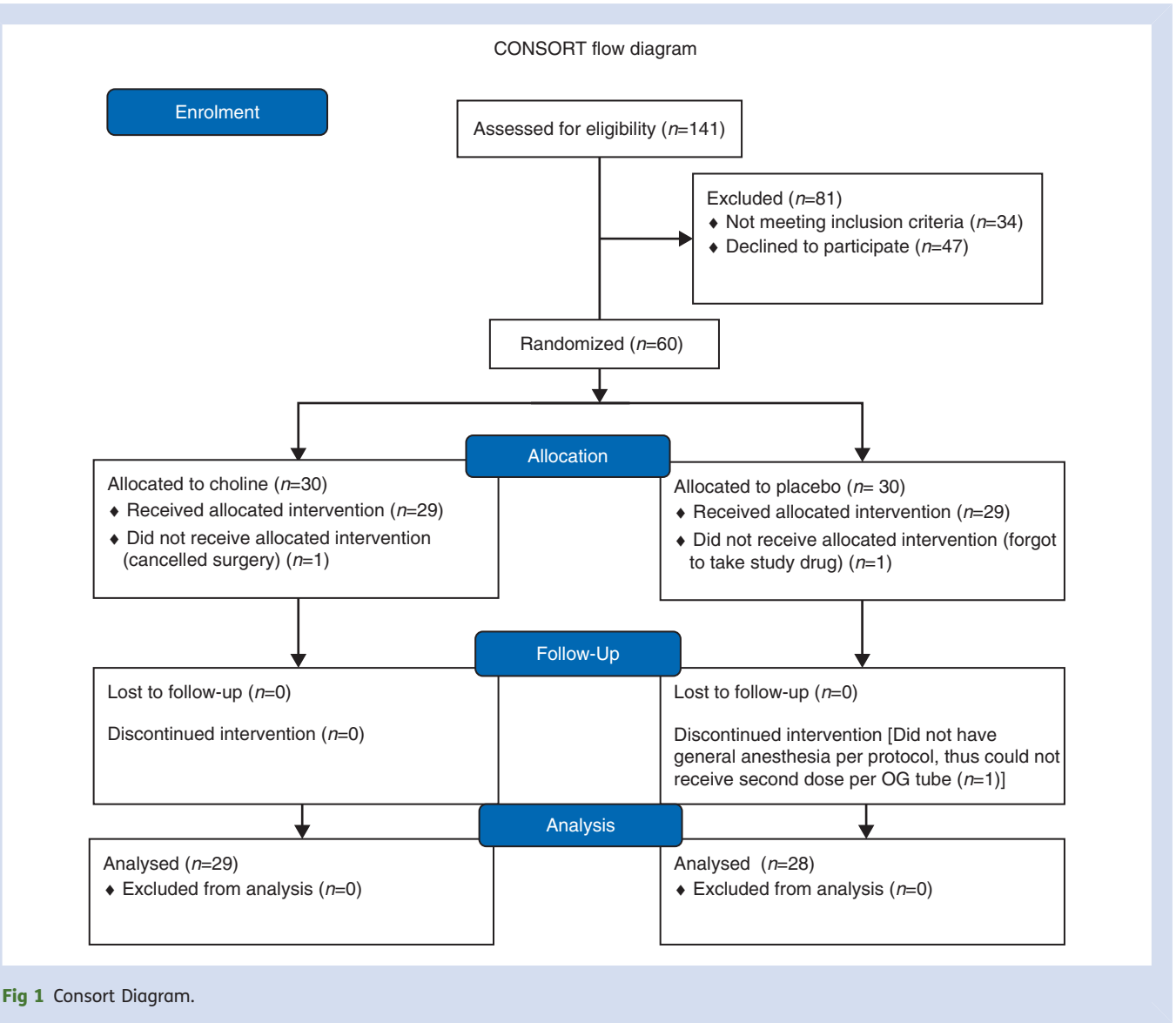

Fig 1 Consort Diagram.