475494 - RESULTS FROM THE PERIOPERATIVE EPIDURAL TRIAL PILOT STUDY

Scott Beattie, MD², Peter Choi, MD¹, Homer Yang, MD³, Norman Buckley, MD⁴, Gregory Bryson, MD³, James Paul, MD⁴

1. Anesthesiology, Pharmacology & Therapeutics, University of British Columbia, Vancouver, BC, Canada

2. Anaesthesia, University of Toronto, Toronto, ON, Canada

3. Anesthesiology, University of Ottawa, Ottawa, ON, Canada

4. Anesthesia, McMaster University, Hamilton, ON, Canada

Introduction: Early randomized controlled trials (RCTs) have suggested that neuraxial blockade may reduce cardiorespiratory complications after non-cardiopulmonary surgery, but two recent large RCTs have been inconclusive.(1,2) Our goal was to answer the following question: “In patients with moderate or high risk for cardiorespiratory events, who are undergoing non-cardiothoracic surgery, does neuraxial anesthesia ± general anesthesia (GA) and postoperative epidural analgesia reduce perioperative mortality and cardiorespiratory events compared to GA and postoperative intravenous (IV) opioid analgesia?” As preliminary work, we conducted a pilot study (ISRCTN 35629817) to determine the rates of enrolment, follow-up, and crossover to assess the feasibility of conducting a large multicentre RCT.

Methods: We obtained approval from the Research Ethics Boards of the participating institutions prior to enrolment. Subjects were eligible if they were ≥ 45 years old, had an expected hospital stay ≥ 48 hours, were undergoing a procedure amenable to epidural analgesia, met one of six risk criteria, and did not have contraindications to neuraxial blockade. After informed consent, subjects were randomly allocated to neuraxial anesthesia ± GA and epidural analgesia (epidural group) or GA and IV opioid analgesia (IV group). The primary outcomes were the rates of enrolment, follow-up, and crossover. We considered a full-scale RCT to be feasible if we were able to recruit $\geq 70\%$ of eligible subjects at an enrolment rate of 1 subject per week per site, complete follow-up in $\geq 95\%$ of randomized subjects, and have $\leq 5\%$ of subjects crossover from their allocated intervention to the alternative. Clinical and safety outcomes, to be used in a full-scale RCT, were secondary outcomes in the pilot study and were adjudicated by a blinded, independent committee. Subjects were followed daily while in hospital and then at 30 days after surgery. Analysis was intention-to-treat.

Results: From May 25, 2005 to August 31, 2006, 494 / 929 screened patients were eligible; 112 / 494 (22.7%) were enrolled. The mean $\pm$ SEM enrolment rate across the four sites was 0.5 ± 0.3 subjects per site per week. Of the 112 consenting subjects, 50 were allocated to the epidural group, 51 were allocated to the IV group, and 11 withdrew prior to randomization. Another three decided not to participate upon entry into the operating room. The remaining 98 / 101 (97.0%) randomized subjects were followed successfully for the 30-day study period. Physicians violated the protocol (i.e., refused to administer the allocated intervention) for three and five subjects in the epidural and IV groups respectively. Within 24 hours of surgery, 9 / 49 (18.3%) subjects in the epidural

group had switched to IV opioid analgesia due to failure to insert the epidural catheter, inadequate analgesia, excessive side effects, or new contraindications. No subjects in the IV group received an epidural catheter for analgesia except the five protocol violations.

Discussion: Of the criteria we defined for the feasibility of a full-scale RCT, only the follow-up rate was successful. The other feasibility outcomes did not meet our preset criteria for success. The results suggest that a large multicentre RCT may not be a feasible design to answer our question of interest.

References: 1) Ann Surg 2001;234:560-71. 2) Lancet 2002;359:1276-82.