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Epidural versus Intravenous Fentanyl: A Problem with Small Sample Size

To the Editor:—Ellis *et al.*¹ designed a careful double-blind study to compare the efficacy of intravenous (iv) versus epidural fentanyl infusions. Their paper was marred by the small sample size and inappropriate conclusions. Only 28 women were involved, with 12 in the iv group and 16 in the epidural group. Statistical analysis by analysis of variance (ANOVA) suggests that with a larger sample, more values would have become significant. A sample size as small as 50 patients with the same mean values and standard errors as the 28 patients reported would have yielded significant differences between the iv and epidural fentanyl infusion groups in the following measurements: 1) 24-h plasma fentanyl levels; 2) pain score at 12 h; 3) maximum sedation score; and 4) volume of medication necessary for pain relief.

Even with the current sample size, 25% of the group receiving iv fentanyl failed to achieve adequate analgesia and so were excluded from further analysis. With a 25% failure rate, the concluding statement of the article, "There appears to be no clinical advantage to epidural infusion over iv infusion of fentanyl for analgesia after cesarean section," seems to be unsupported.

It is hoped that the authors will continue with this study until a large enough patient sample has been evaluated to compare significant clinical differences between iv and epidural fentanyl infusions.

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In Reply:—We appreciate the interest that Dr. Slover and Dr. Palmer have shown in our paper,¹ and their commentary does require further discussion. First, the issue of statistical projection for a larger sample size is valid in theory. A sample size of 50 per group (not 50 total) with the same means and standard deviations (not standard errors) would have yielded differences that were statistically significant. Our statement that an infinite number of patients would have been required to demonstrate such differences was therefore incorrect. We emphasize that the statistical methods were selected prior to institution of the study after a power analysis was performed and that the target sample size originally selected was predicted to demonstrate differences if they existed. The determination of this number is based upon three things: 1) the choice of statistical test; 2) the variability of the data; and 3) the magnitude of the difference it is hoped will be detected. The inability to demonstrate a statistical difference could have been the result of either greater variability than anticipated or an experimental difference that was less than we were able to discriminate. We also would have preferred to have a larger sample size, but since we no longer routinely use the continuous infusion of epidural fentanyl for postoperative cesarean section analgesia due to its time-intensive nature, this was not feasible.

The stated purpose of this study was not to evaluate the efficacy of intravenous (iv) fentanyl as a postoperative analgesic but rather to evaluate side effects and plasma fentanyl levels at effective analgesic levels. The finding that three patients in the intravenous group did not achieve analgesia was presumably the result of higher dosage requirements

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REFERENCE

1. Ellis DJ, Millar WL, Reisner LS: A randomized double-blind comparison of epidural versus intravenous fentanyl infusion for analgesia after cesarean section. *ANESTHESIOLOGY* 72:981-986, 1990

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that could not be administered because of the limit required by our institutional review board. We do not consider this a failure of the technique. Our conclusion, that "there appears to be no clinical advantage to epidural infusion over iv infusion of fentanyl for analgesia after cesarean section," therefore is supported by the data generated in this study when considering side effects and plasma levels.

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