Optimum Dose of Intrathecal Morphine for Labor

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Intrathecal morphine has theoretical advantages for labor analgesia. High dose IT morphine provides analgesia but has significant side effects. When combined with epidural analgesia, low dose IT morphine has been shown to reduce breakthrough pain and postpartum narcotics(1). We hypothesized that mini-dose IT morphine combined with epidural analgesia would improve labor analgesia with minimum side effects. This study is designed to identify the dose-response and side effect profile of mini-dose morphine. This is the interim safety analysis.

Design: Randomized, double-blind, parallel-group assignment dose response study. IRB approval and written consent obtained. Healthy patients in active labor, <6cm dilation were enrolled. Patients were given CSE, in addition to 2mg bupivacaine and 12.5mcg fentanyl, they were randomly assigned to IT morphine of:
- Placebo
- 25mcg
- 50mcg
- 75mcg
- 100mcg. The epidural solution was infused after a negative test dose.

We evaluated need for supplemental epidural medications for breakthrough pain by protocol, and incidence of side effects and need for treatment. Kruskal-Wallis and Chi-Squared used for analysis. Kaplan-Meier used to evaluate median time to dose. P<0.05 was used for significance.

Results: This was a planned interim safety analysis of 50 subjects. Group numbers: A=9, B=8, C=12, D=13, E=6. There were 2 eliminated due to dural puncture and catheter replacement. No difference in demographics or obstetric between groups. No difference in the incidence of pruritis (P=0.83), N/V (P=0.44), or the need for medications for treatment of side effects (P=0.29).

The incidence of breakthrough pain (P=0.64) and rate of breakthrough pain (P=0.08) were not significantly different. By Log-rank analysis of the Kaplan-Meier curve, we found that the median times to first analgesic request were significantly different (P=0.02). (See Figure) The ordered median times (minutes) were: B=120±14, E=186±30, D=198±38, A=251±49, C=265±49.

Discussion: We can identify two points from this planned interim safety and efficacy analysis. First, we cannot distinguish the placebo group from the treatment groups by the incidence of side effects. Thus the study is safe. Second, we found a difference by survival analysis in the median time to analgesic request. This suggests that we may be on the up slope of the dose-response curve. We are likely to have a meaningful result in the final Probit analysis.

Ref:
(1) BJA 2007: 98; 241-245