O2 Determination and quantification of the interaction of local anaesthetics and lipophilic opioids administered intrathecally for labour analgesia

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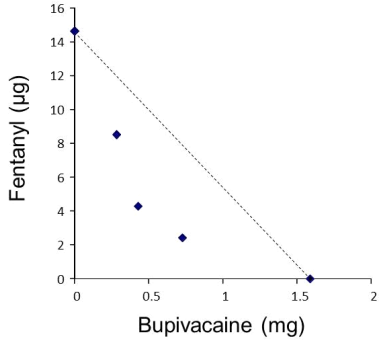
Introduction: Local anaesthetics and opioids are commonly given together during neuraxial labour analgesia with the expectation that the combination is advantageous. However, the nature of their pharmacodynamic interaction has not been fully determined. This study aimed to 1) describe the entire dose-response relation for combinations of intrathecal bupivacaine and fentanyl by determining the pharmacodynamic response surface, and 2) categorize the nature of the interaction (ie. intraadditivity vs additivity vs supraadditivity/synergism).

Methods: In a randomized double-blinded study, with IRB approval and patient consent, 300 labouring women received 1 of 30 different combinations of intrathecal bupivacaine and fentanyl using a combined spinal-epidural technique. Visual analogue pain scores were assessed for 30 min. The primary endpoint was the percentage decrease in pain score from baseline at 15 min. Dose-response data were first analyzed using nonlinear regression as previously described.[1] Data were then pooled to derive a three-dimensional response surface plot.[2] The interaction was categorized by constructing an isobologram using data for a 50% response at 15 min.

Results: A response-surface plot showing the pharmacodynamic interaction of intrathecal bupivacaine and fentanyl was constructed. Analysis of the isobologram revealed that the interaction is supraadditive/synergistic (Figure).

Figure: Isobologram for combinations of intrathecal bupivacaine and fentanyl for a 50% decrease in pain score at 15 min.



Discussion: This is the first study to fully describe the pharmacodynamic interaction of neuraxial local anaesthetic and opioid in humans. The demonstration of a supraadditive/synergistic interaction provides support for the combined administration of these drugs in routine clinical care.

References O

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