The Pharmacokinetic and Pharmacodynamic Effects of Prior Epidural Lidocaine Administration on Extended-Release Epidural Morphine (DepoDur®) in Patients Undergoing Cesarean Delivery

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Background: Extended-release epidural morphine (EREM) provides superior and prolonged post-cesarean analgesia compared to conventional epidural morphine (1). A potential physicochemical interaction with epidural local anesthetics and EREM could negate the sustained-release (2). The aims of this study were to determine the pharmacokinetic (PK) and pharmacodynamic (PD) effects of prior epidural lidocaine administration on EREM.

Methods: Thirty healthy women undergoing cesarean delivery were enrolled in this randomized controlled study. Patients received 8 mg EREM 1 hour after either a combined spinal-epidural (intrathecal bupivacaine 12 mg and fentanyl 20 mcg with no epidural medication; Group 1) or an epidural anesthetic (2% lidocaine with fentanyl 100 mcg; Group 2). Cmax, Tmax and AUC for morphine levels were determined from venous blood measured at 0, 5, 10, 15 and 30 min, and 1, 4, 8, 12, 24, 36, 48, and 72 hrs. PD effects including pain, analgesic use, satisfaction, functional status, and side effects (respiratory depression, nausea, vomiting, pruritus, urinary retention, hypotension) were measured for 72 h post-cesarean. PK parameters were determined by non-compartmental techniques using Phoenix WinNonlin V6.1 and results exported to SPSS V17 for statistical analysis. Statistical significance was considered at P<0.05 for primary PK outcomes and P<0.01 for the multiple PD endpoints.

Results: Epidural lidocaine administration (20-35 ml) 1 hour prior to epidural EREM administration had no significant effect on the PK of EREM. The Cmax, Tmax, and AUC of venous morphine were similar between the groups (Table 1; P>0.05). There were no significant differences in any PD effects including pain scores, analgesic use, or side effects. There was a trend toward more oxygen use in patients who received lidocaine prior to EREM (n=6 vs. n=0) but it was not statistically significant (p=0.02).

Conclusion: Administration of a large dose of epidural lidocaine 1 hour prior to EREM administration did not significantly impact the PK or PD of EREM. Findings from this study suggest that provided 1 hour has passed since lidocaine dosing, patients undergoing cesarean delivery under epidural anesthesia with a lidocaine “top-up” can receive EREM without concerns for a negative interaction on the sustained-release of EREM.

References:

Additional File:

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<thead>
<tr>
<th></th>
<th>Group 1 (n=14)</th>
<th>Group 2 (n=15)</th>
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<tbody>
<tr>
<td>Tmax, hrs: mean (SD)</td>
<td>2.4 (2.0)</td>
<td>0.98 (0.91)</td>
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<tr>
<td>Cmax: ng/ml (SD)</td>
<td>8.3 (7.1)</td>
<td>11.1 (4.9)</td>
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<tr>
<td>AUC_last, h·ng/ml: mean (SD)</td>
<td>37.0 (20.2)</td>
<td>39.9 (12.8)</td>
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SD = standard deviation, no significant differences between groups