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Title: PHARMACOKINETICS OF ROPIVACAINE AND BUPIVACAINE IN PREGNANT EWES

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Ropivacaine is a new amide local anesthetic which appears to hold promise for obstetric use. It is similar to bupivacaine in its potency and duration of action, but its cardiotoxicity is less and not enhanced by pregnancy (1). The present study compares the pharmacokinetics of ropivacaine (R) and bupivacaine (B) in pregnant sheep.

Pregnant ewes, near term of gestation, had intravascular catheters inserted under general anesthesia. After 3-4 days, each ewe was given, in random sequence, 2 intravenous infusion regimens, separated by a one day interval: (1) ropivacaine 0.2 $mg.kg^{-1}.min^{-1}$ for 15 min followed by 0.075 $mg.kg^{-1}.min^{-1}$, over 45 min, (2) bupivacaine, 0.1 $mg.kg^{-1}.min^{-1}$ for 15 min followed by 0.058 $mg.kg^{-1}.min^{-1}$, over 45 min. These infusions were chosen in order to avoid toxicity. The ewes' heart rate and arterial blood pressure were monitored throughout. Arterial blood samples were obtained prior to, at 15 min, the end of infusion (60 min), and at intervals up to 300 min thereafter. Following determination of blood pH and gas tensions, samples were centrifuged, plasma separated and frozen until drug analyses using gas chromatography (limit of sensitivity 5 $ng.ml^{-1}$). "SIMPLEX", a nonlinear regression computer program, was used to derive pharmacokinetic indices. Paired Student's "t" test or ANOVA were applied to detect statistically significant differences ($p<0.05$). Results are expressed as the mean±SD.

Five animals have been studied thus far. All were in good general condition throughout the experiments. Infusion of either local anesthetic did not alter the ewe's heart rate, mean arterial blood pressure, pH or gas tensions. The plasma concentrations of R and B at the end of infusion were similar, 2.24±0.47 and 1.8±0.21 $\mu g.ml^{-1}$, respectively. By 300 min these had declined to 0.2±0.09 $\mu g.ml^{-1}$ for R and 0.2±0.05 $\mu g.ml^{-1}$ for B. The elimination half-life ($T_{\frac{1}{2}\beta}$) of R was significantly shorter, 104±25 vs 129±23 min for B. The volumes of distribution at steady state (Vdss) were similar (3.0±1.2 and 2.8±0.8 $L.kg^{-1}$). There was a trend toward a faster clearance (Cl) for R then B, 25±13 vs 17±6 $ml.min^{-1}.kg^{-1}$, but this difference failed to achieve statistical significance ($p=0.06$).

These data indicate that, in pregnant ewes, R has a shorter $T_{\frac{1}{2}\beta}$ than B, probably due to a faster Cl. Similar findings were obtained in nonpregnant volunteers (2). Assuming the results of our study are applicable to pregnant women, repeated injections of R should result in lower accumulation than with B.

References
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A830

TITLE: AN IN-VITRO ASSESSMENT OF AMNIOTIC FLUID REMOVAL FROM HUMAN BLOOD THROUGH CELL SAVER PROCESSING

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Introduction:
Major obstetric hemorrhage accounts for approximately 13.4% of maternal mortality in the United States.[1] The risks associated with transfusion of non-autologous bank blood include infection (e.g., hepatitis, AIDS, Yersinia enterocolitica), transfusion reaction, and Rh sensitization.[2] Massive intraoperative obstetrical hemorrhage may risk amniotic fluid contamination from the surgical field. Amniotic fluid (AF) may contain lanugo hair, vernix caseosa, meconium, and fetal cellular debris. These may potentially cause cardiovascular collapse and/or DIC if significant quantities enter the maternal circulation.[3] Patients with clinical symptoms of Amniotic Fluid Embolism (AFE) tend to have higher quantities of fetal debris in their circulation than non-affected patients.[4] By using the cell saver wash cycle AF debris may be effectively reduced or eliminated. This in-vitro study was designed to determine if the Shiley Dideco 795 P Cell Saver could adequately clear gross amniotic fluid from human blood.

Methods:
Sterile amniotic fluid was obtained from healthy ASA I and II parturients undergoing elective cesarean sections. Six samples of amniotic fluid in concentrations of 20% and 25% were mixed with outdated whole bank blood and six samples of amniotic fluid in concentrations of 20% and 33% were mixed with fresh whole blood from patients with hemochromatosis. These samples were passed through a 40 micron cardiotomy filter, primed at 300 cc/min, and washed with 2 liters of normal saline using the Shiley Dideco 795 P cell saver. Post wash samples from the bank blood mixture and pre and post wash samples from the fresh blood mixture were tested for alpha fetal protein (AFP) concentrations (Kallestad AFP OB Radioimmunoassay with a maximum sensitivity of 2.2 international units per milliliter). Cell smears for fetal squamous cells were performed using Giemsa Wright staining.

Results:
Six pre-wash samples with 20% and 33% AF had AFP levels which ranged from 36-83 international units per milliliter. All twelve post-wash samples had alpha fetal protein levels of zero. Pre-wash Giemsa-Wright Staining had cell concentrations ranging from 26-34 squames per 4 microliter, whereas post-wash cell concentrations ranged from 1.5-15 squames per 4 microliters. No trophoblasts, lanugo hair, or vernix caseosa were seen.

Conclusion:
We conclude that when AFP and fetal debris are used as markers for AF, cell saver processing appears to completely remove AFP and reduce the quantity of fetal debris. Presently, it is unclear which markers or substances within AF are the etiologic triggers responsible for the signs and symptoms of AFE.[3]

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