Easily injectable depot preparation of local anesthetics in
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Anesthesiology, V 104, No 1, Jan 2006
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Duration of Block with
Investigators Study Effects of Remifentanil
Given Prior to Cesarean Section. Ngan Kee et al. (page 14)
Anesthesiologists have reported cases of remifentanil used
during induction of general anesthesia for cesarean section
in women with preeclampsia and other conditions, to mod-
ulate maternal heart rate and blood pressure. However, no
controlled studies to date have monitored effects on neo-
nates at birth after use of remifentanil for induction pur-
poses. Ngan Kee et al. devised a randomized, double-blind,
controlled study to investigate the matter.
Enrolling 40 women with singleton pregnancies sched-
uled for elective cesarean section, the team randomly
allowed the participants to receive an intravenous bolus
of either 1 μg/kg remifentanil or saline immediately
before induction of general anesthesia. Patients received
ranitidine or famotidine orally the night before their
scheduled procedures. Using standard monitoring, the
team assessed blood pressure, heart rate, and mean ar-
terial pressure throughout the study period. After deliv-
er, neonates were assessed by a pediatrician blinded as
to maternal group assignment. Time to sustained respi-
ratory, any resuscitative measures required, and Apgar
scores at 1 and 5 min after birth were all recorded.
The women receiving remifentanil registered a smaller
increase in systolic arterial pressure after induction than
did those receiving saline solution. The Apgar scores and
time to sustained respiration were similar between the
two groups of neonates. However, two neonates deliv-
ered from mothers in the remifentanil group were con-
sidered clinically depressed and were given naloxone.
The single bolus of remifentanil effectively attenuated
hemodynamic changes after induction of anesthesia and
tracheal intubation in the mothers. However, because
the drug crosses the placenta and produced side effects
in the neonates, the researchers advise that the drug should
be used for clear maternal indications only when adequate
facilities for neonatal resuscitation are available.

Duration of Block with
Investigators continue to search for the ideal vehicle
for accomplishing long-term nerve blocks for the treat-
ment of chronic pain. In this issue, Söderberg et al.
report on their efforts to develop a physically stable and
easily injectable depot preparation of local anesthetics in
which the concentration could be varied between 0 and
100%. The team prepared six lipid formulations, contain-
ing 2.0, 5.0, 20, 40, 60, or 80% of lidocaine:prilocaine
(1:1, by weight) in medium-chain triglyceride. All formul-
ations were oily liquids at room temperature and could
be injected through a 29-gauge needle. Saline solutions
of lidocaine:prilocaine HCl were prepared at 0.40 and
2.0% strength, and a sterile 99.5% ethanol solution was
used as an active control in one experiment.
In three separate randomized experiments, the team
assessed the duration of sciatic nerve block and local
neurotoxicity after administration of 10 different prepara-
rations. Based on the outcome of nerve block experi-
ments, two formulations (the 20% and 60% lidocaine:
prilocaine in medium-chain triglyceride) underwent
further studies. Rats receiving the 20% formulation dem-
strated a threefold duration of sensory block com-
pared to those receiving the 2% aqueous solution, while
rats receiving the 60% formulation experienced blocks
180 times those of the aqueous solution group. In the
higher concentration formulations (80% and 100%) all
animals still showed nerve block 2 weeks later. How-
ever, lidocaine:prilocaine formulations of 60% or greater
produced significant neurotoxic effects, as did the etha-
nol solution. In vivo investigations of time for 50% re-
lease revealed a clear difference between the aqueous
solution and lipid formulations. The in vivo release of
local anesthetic, the team found, could be approximately
predicted from in vitro data for the lower formulation
(20%) but not the 60% formulation. Although the possi-
bility of using a high-concentration local anesthetic depot
formulation for long-term nerve blocks exists, the authors
cautions that further investigation is needed before these
could replace the standard use of ethanol or phenol.

Susceptibility to Ventilator-associated
Lung Injury after Endotoxin Exposure. Schreiber et al. (page 133)
Schreiber et al. designed a study to investigate the
relationship between transient systemic inflammation
and lung injury after mechanical ventilation. They ex-
posed one group of rats to a transient endotoxin chal-
lenge by injecting them with a nonlethal dose of Esche-
birchia coli endotoxin. After 24 h, both control
(phosphate buffered saline)-treated and endotoxin-treated
rats were randomized to undergo either no mechanical
ventilation or mechanical ventilation with varying tidal vol-
umes (tidal volumes of 8, 24, 27, or 30 ml/kg body weight). There were 10 rats in each treatment group.

Animals who received endotoxin but were not in a ventilation group showed no symptoms of clinical illness 24 h later, although their lung neutrophil counts were increased. For rats undergoing mechanical ventilation, body temperature was maintained at 38°C, and heart rate, arterial and central venous blood pressures, peak airway pressure, and arterial blood gases were recorded every 30 min. After 4 h of mechanical ventilation, the animals were killed and their lungs harvested for histologic examination.

Compared to the animals in control groups, those receiving high tidal volume ventilation showed stronger pulmonary inflammatory responses and more severe lung injury. This injury was demonstrated by impaired oxygenation, increased lung wet-to-dry weight ratios, and increased levels of protein, neutrophils, and cytokines in lung lavage fluid. Animals treated with endotoxin who later received low tidal volume ventilation had an inflammatory response but did not show pulmonary impairment. The 24-h delay after systemic injection of endotoxin, in this animal model, resulted in an increased susceptibility to the deleterious effects of increasing tidal volume. Avoiding high tidal volume in patients who have recovered from a period of endotoxemia might be advisable.

Deciphering the Analgesic Action of Preoperative Cyclooxygenase-2 Inhibitors. Fornai et al. (page 152)

Fornai et al. designed a double-blind randomized trial to assess whether prostaglandin production at the surgical site accounts for the analgesia associated with use of cyclooxygenase-2 (COX-2) blockade in the preoperative period. They administered 50 mg rofecoxib (a selective COX-2 inhibitor), 550 mg naproxen (a nonselective COX-1/COX-2 inhibitor), or placebo preoperatively to patients who were scheduled to undergo removal of an impacted third molar.

The team collected gingival specimens during tooth removal and 240 min after surgery. They also evaluated patients’ subjective pain using categorical and visual analogue scales every 30 min beginning an hour and a half after surgery. Cyclooxygenase-1 and COX-2 mRNA expression was examined by reverse-transcription polymerase chain reaction in the gingival specimens collected.

The team found that pain intensity and prostaglandin E₂ production in the placebo group increased throughout the observation period. Preoperative naproxen prevented pain and decreased prostaglandin production at all time points. Rofecoxib produced pain relief throughout the entire observation period, and reduced prostaglandin production from 150 min onward, compared to placebo. At the end of the observation period, COX-1 mRNA expression was unchanged, whereas COX-2 mRNA was significantly induced. Although preoperative administration of a selective COX-2 inhibitor confers effective control of postoperative oral surgical pain, the selective blockade of inducible COX-2 at the peripheral level does not entirely explain the analgesic action of the drug in the postoperative period.

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