

Title: DURAL TRANSFER OF PHENOL FOLLOWING EPIDURAL INJECTION IN CYNOMOLOGUS MONKEYS

Authors: R.R. Concilus, M.D., C.S. Sehlhorst B.S., D.D. Denson, Ph.D., J. Katz, M.D., R.V. Gregg, M.D.

Affiliation: Dept. of Anesthesia, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267-0531

Introduction. Injection of phenol into the epidural space is utilized as a technique for the management of a variety of painful conditions. While the mechanism of the resulting analgesia is not known, it is presumed to be from extradural action of the phenol. The amount of dural transfer of phenol is believed to be small minimizing the role of the destructive action of phenol on spinal structures (1). This study was conducted to measure the dural transfer of phenol following epidural injection in cynomologus monkeys.

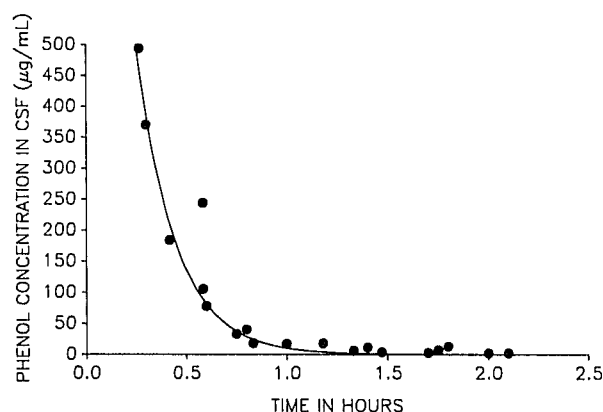
Methods. This study was approved by the Institutional Animal Care and Use Committee. Five male cynomologus monkeys weighing 5.6 ± 0.4 kg were anesthetized with ketamine supplemented with halothane N₂O and oxygen. A lumbar epidural catheter (PE-10) was placed at the L4-5 or L5-6 interspace using a loss of resistance technique. A similar catheter was then placed in the subarachnoid space one vertebral interspace rostral to the site of the epidural catheter. Localization of the epidural catheter was confirmed in all animals radiographically by injection of 2 mL of Omnipaque-240. Following confirmation of the epidural catheter, the animals were allowed to fully awaken in a primate restraining chair. 0.5 mL of 8% phenol in Renografin were then injected via the epidural catheter over thirty seconds. 35 μ L samples of CSF were drawn over two hours at fifteen minute intervals as permitted by technical considerations. Phenol concentrations were measured by gas chromatography. Composite phenol concentration-time data were fit using a nonlinear iterative procedure (PC-Nonlin). Peak phenol concentrations and elimination half-lives of phenol in CSF were calculated from the best fit of the data. The fraction of the dose transferred (F_D) was estimated by the method of Moore et al. using the following equation (2):

$$F_D = (P/k_a) \cdot (A/V) \cdot 100$$

where P is the dural permeability constant (0.0047 (Moore et al.) or 0.0061 (Racz et al.); k_a is the systemic absorption rate constant estimated using an absorption half-life of twenty minutes; V is the volume injected into the epidural space and A is the calculated surface area of dura exposed to phenol. All data are presented as mean \pm SD.

Results. Vertebral lengths in the animals in this study ranged from 25-35 cm. Injection of 2mL of Omnipaque-240 into the epidural space resulted in a spread of 10 ± 1 vertebral segments without evidence of leakage into the subarachnoid space. From these results, the surface area of dura exposed to phenol was calculated to be 4.25 cm². Insertion of this value into the above equation, gave an estimated F_D of 23-29%. The composite phenol concentration-time data are presented in the figure. It is clear from this figure that phenol rapidly crosses the dura with the peak concentration occurring prior to fifteen minutes. Analysis of these data gave a peak

phenol concentration of 1845 ± 466 μ g/mL and an elimination half-life of 8 ± 1 minutes. The total amount of phenol transferred was calculated to be 5166 ± 1304 μ g/mL which represents $12.9 \pm 3.3\%$ of the administered dose.



Discussion. Our value of 12.9% dural transfer of phenol may be a slight overestimate because our sampling protocol did not allow us to adequately describe the early absorption and/or diffusion process(es). In this dynamic model, the F_D of 12.9% is consistent with the 14% reported by Racz et al. using an *in vitro* design. The F_D reported here is however well below that estimated using the method of Moore et al (2). Our estimation of a elimination half-life of 8 ± 1 minutes is consistent with the human data of Ichiyanagi et al. and support the hypothesis of Racz et al. that significant accumulation of phenol would not continue to occur because of concomitant rapid elimination from the subarachnoid space. This study demonstrates the need to determine the minimum neurolytic concentration with respect to spinal nervous structures so that a maximum amount of phenol for a single epidural injection can be scientifically defined.

References

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