Title: PHARMACOKINETICS OF 2% RECTAL METHOHEXITAL IN CHILDREN

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Introduction. Rectal methohexital is a safe, pleasant technique for the induction of anesthesia in young children. Administration of 25 mg/kg 10% methohexital results in the onset of sleep within 15 minutes in about 85% of patients.[1,2] However, it has been reported that 15 mg/kg 1% methohexital is as effective as 25 mg/kg of a 10% solution for induction of anesthesia[3] and that use of a 2% solution results in higher peak plasma methohexital concentrations.[4] Because changes in the volume and concentration of a methohexital solution alter its pharmacokinetics, the optimal dose of methohexital for induction of anesthesia has not been determined. Therefore, the purpose of this investigation was to compare the clinical effect and plasma methohexital concentrations achieved following rectal administration of four doses of 2% methohexital.

Methods. Sixty children were studied after obtaining informed parental consent. Each child was randomly assigned to receive 15, 20, 25 or 30 mg/kg 2% methohexital. The drug was administered rectally using a soft, plastic catheter while a parent comforted the child until the onset of sleep. Sleep was defined as loss of consciousness, unresponsiveness to verbal stimuli and absence of voluntary movement when unstimulated. Time from administration of methohexital until the onset of sleep was recorded by a blinded observor. Each child was then transferred to the operating room and anesthesia continued with halothane and nitrous oxide in oxygen. Children not asleep fifteen minutes following methohexital administration underwent inhalation induction of anesthesia. Blood samples were collected at 15, 30, 45 and 120 minutes following drug administration, centrifuged, and the plasma frozen for later determination of methohexital concentration using gas chromatography. Results are expressed as mean ± S.E.M. Statistical significant ($P < 0.05$) was determined using Chi-square analysis for the time to the onset of sleep and analysis of variance and t-test with Bonferroni's adjustment for demographic data and plasma methohexital concentrations.

Results. The mean age and weight did not differ significantly among the groups. The speed and reliability of induction was significantly greater in children receiving 25-30 mg/kg 2% methohexital when compared to those children that received 15-20 mg/kg (Figure 1). Also, plasma methohexital levels were significantly higher at all time periods in the children that received 30 mg/kg and at 15, 30 and 45 minutes in the children that received 25 mg/kg when compared to children that received 15 mg/kg (Figure 2).

Figure 1

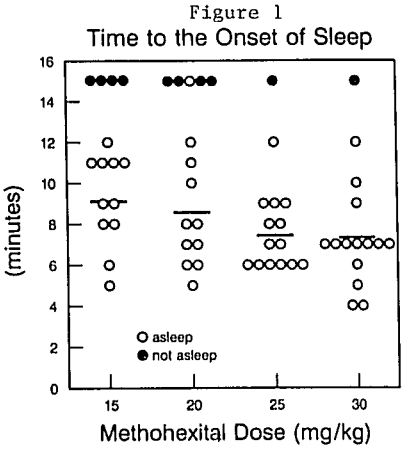
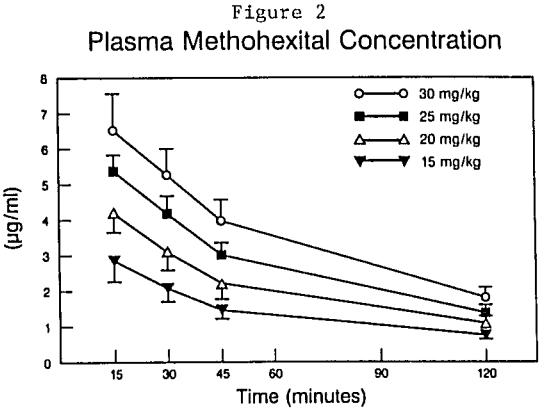


Figure 2



Discussion. The effectiveness of rectally administered methohexital depends upon a complex interaction between the volume and concentration of the solution administered and the site of absorption within the rectum. From the results of this study we conclude that 2% rectal methohexital is an effective alternative to the use of a 10% solution for induction anesthesia in children and that administration of 25-30 mg/kg 2% rectal methohexital results in higher plasma concentrations and a more rapid and reliable onset of sleep than does the use of 15-20 mg/kg.

References.

1. Goresky GV, Steward DJ: Can Anaesth Soc 1979;26:213-215.

2. Liu LMP et al: Anesthesiology 1980; 53:343-345.

3. Laishley RS et al: Can Anaesth Soc J 1986; 33:427-432.

4. Forbes RB, Vandewalker GE: Anesthesiology 1986:A420.