Title: RECTAL MUCOSAL INJURY AFTER RECTAL PREMEDICATION WITH METHOHEXITAL

Authors: Allen J. Hinkle,M. D. and Chris M. Weinlander, M. D.

Affiliation: Department of Surgery (Anesthesia) and Maternal and Child Health, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire 03756

Introduction. Certain anesthetics, such as methohexital, thiopental and etomidate, produce pain during intravenous (IV) injection. The incidence of pain on administration of methohexital has been reported to be 60%.[1] The etiology of this discomfort has been attributed to a local inflammatory response. It has been well documented with inadvertant intra-arterial (IA) injection of thiopental. Concentrations greater than 25 mg/ml produce a chemical endarteritis. The severity of this response has been found to be directly proportional to drug concentration.

Painful IV administration of methohexital has not been shown to lead to thrombophlebitis. This may be attributable to the concentration used intravenously (10 mg/ml) as well as the dilution of the drug by IV solutions and venous flow. Rectal methohexital has been used in high concentrations (100 mg/ml) for a number of years in children. When injected it remains in contact with the rectal mucosa for an extended period.

We became interested in the local irritant effect due to the incidence of complaints of rectal pain after rectal methohexital. This study uses mice to investigate the in vivo effects of rectal anesthetic agents on the mucosa.

Method. Fifty CD-1 25 gm mice were studied. They were randomly assigned to one of seven groups.

Group 1: Control. No rectal catheter or injection
Group 2: Rectal catheter/no injection
Group 3: Rectal normal saline (NS.) 10 ul injectate
Group 4: Rectal methohexital 10%. 10 ul
Group 5: Rectal ketamine 5% commercial prep. 10 ul (9 mg/Kg)
Group 6: Rectal ketamine 5% without preservative. 10 ul (9 mg/Kg)
Group 7: Rectal benzethonium chloride (BCl) 0.1mg/ml (ketamine preservative) 10 ul

pH and osmolarity determinations were made on all solutions.

A 2.5 cm plastic catheter was used to administer the solutions rectally. Two animals from Group 2-7 were sacrificed with ether at 2 hrs, 6 hrs, 24 hrs and 1 week following the injection. The rectum was excised and histologic sections made with hematoxylin-eosin staining. The microscopic sections were graded as to degree of mucosal change including inflammation, hemorrhage and/or ulceration.

Results. Rectal methohexital caused mucosal inflammatory changes that were initially present at 2 hrs and persisted through 1 week following injection (Table 1). The extent of damage is shown in Figure 1 B.

Commercially prepared ketamine, pure ketamine and the solution of BCl produced no mucosal abnormalities, except for edema.

Discussion. Of the agents studied methohexital produced a marked mucosal inflammatory response on rectal administration. This may be attributable to the extreme alkalinity, hyperosmolarity or to a property of the drug itself. The latter possibility is supported by work comparing the IA injection of thiopental with solutions buffered to a similar pH (10.6). Thiopental consistently produced necrosis while the alkaline solution alone did not.[2] No studies show the effects of solutions of varying osmolarities when injected IV, IA or rectally.

The concentration of methohexital used rectally is ten times that recommended for intravenous use. Studies of inadvertant IA thiopental have shown a direct relationship between concentration and damage.

The extended contact between the drug and the rectal mucosa may also contribute to the extent of damage. Unlike IV injections, there is no dilution of the drug from the mucosal surface.

Commercially prepared ketamine, pure ketamine and the preservative BCl did not produce mucosal changes. This concurs with the clinical observation of a lack of complaints after rectal use. It may be attributable to their more physiologic physicochemical characteristics.

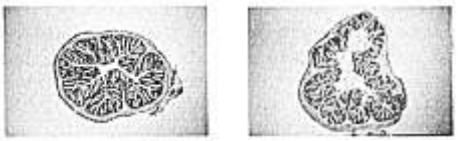
A variety of anesthetic drugs are administered rectally in addition to those reported in this study.[3] These agents have been deemed safe for rectal instillation. Clearly, further work needs to be done to elucidate the extent of mucosal injury produced by these medications also.

TABLE 1:

Group	pH	osm	I	U	H	E
2	-	-	0	0	0	0
3	6.5	285	0	0	0	0
4	10.0	819	+++	++++	+	+
5	6.0	381	+	0	0	+
6	6.0	604	+	0	0	+
7	6.5	285	0	0	0	0

I = inflammation, U - ulceration, H = hemorrhage, E = edema

FIGURE 1:



A - Control B - 6 hrs Post-Brevital

References.

1. Taylor C, Stoelting VK: Methohexital sodium-a new ultrashort acting barbiturate. Anesthesiology. 21:29-34, 1960
2. Kinmonth J, Shepherd R: Accidental injection of thiopentone into arteries. Brit Med J 2:914, 1959
3. Ahn NC, et al: Preanaesthetic medication with rectal diazepam in children. Acta Anaesth Scand