Effects of Cyclopentolate Eyedrops on Gastric Secretory Function in Pre-term Infants

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Abstract: Because of a report of necrotizing enterocolitis and death of a neonate from cyclopentolate eyedrops, we prospectively studied the effects of cyclopentolate 0.5% and 0.25% ophthalmic solutions and of a placebo on gastric volume and acid secretions in 20 pre-term infants. Placebo and cyclopentolate 0.25% eyedrops had no significant effect on the tested gastric functions. However, cyclopentolate 0.5% eyedrops significantly decreased gastric acid secretion and volume. Since this effect may predispose to the development of gastroenteritis, we recommend that cyclopentolate 0.5% be avoided in preterm infants; a weaker concentration of cyclopentolate eyedrops, however, can be used for mydriasis. [Key words: cyclopentolate, gastric secretory function, infants, mydriatics.] Ophthalmology 92:698-700, 1985

Systemic effects of mydriatic agents have been previously described in low-weight infants.1 Due to the significant blood pressure elevation engendered by phenylephrine 2.5% eyedrops in the low-weight neonate, we have recommended that lesser concentrations of phenylephrine eyedrops be used in this population.2 However, the upper limit of some cycloplegic agents that can be safely administered to infants has not been established. In 1973, Bauer and colleagues felt that cyclopentolate 1.0% was associated with anticholinergic gastrointestinal effects in two preterm infants, one of whom subsequently died of necrotizing enterocolitis.3

We wanted to determine if cyclopentolate eyedrops do affect gastrointestinal function of the pre-term infant and whether there is a concentration that does not affect this function. To do so, we measured gastric volume and basal acid output before and after 0.25% and 0.5% concentrations of cyclopentolate eyedrops and placebo were administered.

MATERIALS AND METHODS

The study protocol was approved by the Human Subjects Committee of Harbor/UCLA Medical Center on July 12, 1983 and approval was renewed on July 24, 1984. Informed written consent was obtained from the parents or guardians of each infant prior to study.

Twenty healthy pre-term infants (12 females) weighing less than 2100 g were enrolled in the study. All infants were born with gestational ages of 35 weeks or less by Dubowitz score4 (mean ± SD = 31 ± 2 wk; range, 27-35 weeks). Birthweights ranged from 680 to 1840 g (mean ± SD = 1233 ± 390 g). Postnatal ages at the time of study ranged from 1 to 15 weeks (mean ± SD = 6 ± 4 weeks). Small for gestational age infants and infants with acute intercurrent illness were excluded from the study. All of the subjects had received oxygen for at least six hours during their hospital course, but none was receiving oxygen at the time of study. In all infants, enteral feedings were discontinued 3 hours prior to testing.
Acid output was measured by the standard aspiration method previously described. A vented 10 Fr sump tube was passed through the oropharynx into the stomach. The stomach was emptied of residual contents and placement of the tube in the most dependent portion of the stomach was verified by the immediate recovery of at least 90% of a bolus of water (5 ml/kg). When milk stained gastric residuals were present, the stomach was lavaged with 5 ml/kg sterile water one to three times, or until the aspirate was clear by inspection. Gastric contents were thereafter aspirated manually, and collected in 15 min aliquots. The initial 15 min sample was discarded, and four 15-minute baseline samples were collected and saved to determine basal acid output (BAO). After basal samples were collected, two drops of the tested solutions were administered to each eye 5 minutes apart. Four additional 15-minute samples were collected and saved for comparison with those obtained before eyedrop administration. Infants were assigned randomly to receive one of three eyedrop preparations:

0.9% NaCl (placebo control), 0.25% cyclopentolate, or 0.5% cyclopentolate. Cutaneous absorption of these medications was minimized by wiping away excess fluid from the periocular area.

All samples were refrigerated at 4°C and analyzed within 48 hours. For each sample, volume and pH were recorded, and hydrogen ion concentration was measured by titration to pH 7.0 with a Radiometer TTT60 titrator and ABU60 autoburette (Radiometer, Copenhagen, Denmark).

Results of acid secretory studies were expressed in ml/kg/hr and μmol/kg/hr because volume and acid output were directly proportional to body weight in previous studies of pre-term infants.

Statistical evaluations comparing the three groups were accomplished with the unpaired t-test. Comparisons of results within each group before and after eyedrops were done with the paired t-test.

**RESULTS**

The three groups of infants did not vary significantly in weight, basal acid, or volume output at the time of study (Table 1).

In the second hour of gastric aspiration, volume decreased (after the eyedrops were administered) in all three groups. However, this trend was significant only for infants receiving cyclopentolate 0.5% (Fig 1). In contrast to the placebo and cyclopentolate 0.25% groups, whose volume decreased by 27% and 21% respectively, cyclopentolate 0.5% caused a 58% inhibition of volume secretion compared with the first hour volume ($P < 0.005$).

In the hour following eyedrops, acid output hardly changed in the first two groups but decreased significantly in the group receiving cyclopentolate 0.5% (Fig 2). Acid
output was inhibited after cyclopentolate 0.5% by 73% ($P < 0.01$). Although no infant was achlorhydric during the basal hour of study, two infants in the placebo group and one infant in the 0.25% cyclopentolate group were subsequently achlorhydric. However, four of eight infants developed achlorhydria following cyclopentolate 0.5% administration.

**DISCUSSION**

Gastric acid provides a barrier to bacterial colonization of the small bowel. Acid denatures many proteins, and stimulates pepsin activity, digesting proteins. Gastric acid probably serves important immunologic functions in the pre-term infant by reducing the number of foreign antigens and bacteria passing from the stomach into the intestine. Thus the presence of acid in the stomach of the pre-term infant may be important in decreasing the susceptibility to enteric infections. Conversely, a reduction in acid content may enhance the development of enterocolitis. Our finding that cyclopentolate decreases gastric acid secretion supports the contention of Bauer and colleagues that cyclopentolate eyedrops may have engendered necrotizing enterocolitis resulting in the death of a neonate. Bauer and co-workers concluded that cyclopentolate 1% should be avoided, and that the 0.5% concentration be used instead. However, we would go further because of our finding of an anticholinergic action of cyclopentolate 0.5% on gastric secretion. We have not yet investigated other possible anticholinergic effects of eyedrops that might adversely affect gastrointestinal function, such as decreasing salivary, tongue lipase, and pancreatic secretions and inhibition of gastrointestinal motility.

Punctal occlusion at the time of eyedrop administration as studied by Zimmerman may reduce the systemic effects of cyclopentolate 0.5% eyedrops. However, the small size of the conjunctival fornix in the infant, causing spillover of eyedrops onto the eyelids, combined with the difficulty of maintaining pressure on a baby's punctae, may negate some of the benefit of punctal occlusion.

This study provides evidence that cyclopentolate eyedrops can significantly inhibit gastric volume and acid output in infants. However, this effect was only engendered by the 0.5% concentration, and not by the 0.25% concentration. On the basis of available information, it would seem prudent to recommend that in pre-term infants cyclopentolate eyedrops should be used in concentrations of 0.25% or less. The commercially available combination of phenylephrine 1% and cyclopentolate 0.2% on the basis of our studies would appear to be safe.

**REFERENCES**