Effect of Benzalkonium Chloride on Urinary Mucus Concentration Following Augmentation Ileocystoplasty in Mice

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Background/Purpose: Ileocystoplasty is a popular technique used for treatment of low-capacity urinary bladders. One of its major downsides is the ability of the intestinal mucosa to secrete mucus, with its related urinary complications. Benzalkonium chloride is an irreversible ganglion blocker. Its local application to the augmenting ileal patch could reduce the acetyl choline-mediated mucus secretion. The aim of this study was to evaluate the effect of benzalkonium chloride on urinary mucus concentration following augmentation ileocystoplasty in mice.

Materials and Methods: Ileocystoplasty was performed experimentally in a group of albino mice. Benzalkonium chloride was applied locally to the ileal patch in half of them. Twenty survivors from each group were evaluated by 24-hours urine collection and mucus concentration assessment. Histopathological evaluation of the urinary bladders was carried out three weeks later.

Result: In the benzalkonium group, the mean urinary mucus concentration was significantly lower than the control group (P<0.001). In the former group, the histopathological examination revealed no reactions that might have resulted from benzalkonium application, together with a marked reduction in the mucus secretion activities in all specimens.

Conclusion: Benzalkonium chloride might be used to reduce the incidence of mucus-related complications in ileocystoplasty. Its use in humans, as well as the adverse effects due to systemic absorption, is still to be investigated.

Index Word: Ileocystoplasty, Benzalkonium chloride

INTRODUCTION

The use of gastrointestinal patches has been applied increasingly in the reconstruction of the lower urinary tract. Providing a large-capacity and good-compliant urinary reservoir, ileocystoplasty has gained much popularity among pediatric urologists in treating low-capacity, poor-compliant urinary bladders. However, the intestinal mucosa is capable of secreting mucus even if transposed in other organs. The average daily mucus production from both ileum and colon when used as a cystoplasty segment is 35-40 g. This does not reduce substantially with time, despite the time-related villous atrophy of the
intestinal patch mucosa. This, in turn, causes many complications including urinary tract infections (UTI), difficulties in clean intermittent catheterization (CIC), and urolithiasis.

Several methods had been advocated in order to minimize the unwanted effects of the secreted mucus including the use of oral ranitidine, urea, and N-acetyl cysteine for intravesical wash, with variable degrees of success. Benzalkonium chloride is a potent irreversible ganglion blocker that can produce its action locally. On the account that a considerable amount of intestinal mucus secretion relies on enteric ganglion reflexes, benzalkonium chloride was applied locally on the augmenting ileal patch in rats undergoing experimental ileocystoplasty, and its effect on mucus secretion was evaluated.

**PATIENTS AND METHODS**

A classic ileocystoplasty technique was performed experimentally in a group of albino mice. In half of them (group A), 2 ml of 1/100 Benzalkonium chloride were applied locally for 10 seconds and then washed out from the ileal patch. This step was omitted in the other half (control group B). Twenty mice of the survivors from each group were evaluated by 24-hours urine collection (collected through the metabolic cage), and mucus concentration assessment using a spectrophotometer. After three weeks, the mice were sacrificed, and the new bladders were sent for histopathological evaluation. This included measuring the mucus secretion activities (reported as basal goblet cells concentration and mucus lake distribution), in addition to evaluation of the possible local pathological reactions to the application of benzalkonium.

**RESULTS**

The mean urinary mucus concentration in group A mice (the benzalkonium group) was $0.15 \pm 0.09$ mg/ml, which was significantly lower than that of group B mice (the control group) $0.96 \pm 0.24$ mg/ml ($P<0.001$). Also, the histopathological examination revealed no pathological reactions that might have resulted from benzalkonium application, together with a marked reduction in the mucus secretion activities in all specimens in group A (Fig 1,2).

**DISCUSSION**

Two distinct mechanisms of mucus secretion exist in the small intestinal mucosa. The rapid phase, which relies on the basal goblet cells and is under control of acetyl choline, and the slow phase, that arises from the surface goblet cells, and is independent from any neural control. Elimination of mucus production is not an easy task and may indeed be inadvisable. Mucus provides a protective layer to the bowel epithelium in its natural environment, and an intact mucus layer may be important in protecting the bowel patch from contact with the urinary carcinogens and other harmful substances. Therefore, to avoid the complications of excess secretion, it seems ideal to eliminate the rapid mucus secretion phase alone. This will preserve the base-line slow phase secretion to retain its needed protective effect. Benzalkonium chloride is known to be an irreversible ganglion blocker. Its local application to the augmenting ileal patch resulted in reducing the acetyl choline-mediated mucus secretion, without producing any harmful effects on the patch. Reduction of ileal mucus secretion after ileocystoplasty should invariably lower the incidence of mucus-related complications.

**CONCLUSION**

Local application of benzalkonium is easy, and results in marked reduction in the mucus secretion of the intestinal patch after ileocystoplasty in mice with no
harmful local effects. Therefore, it might be used to reduce the incidence of mucus-related complications. However, its use in humans, as well as the adverse effects due to systemic absorption is still to be investigated.

REFERENCES


