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TOPICALLY APPLIED NSAID IS LOCALLY DELIVERED TO THE LOWER URINARY TRACT WHERE IT SUPPRESSES EXCESSIVE PRODUCTION OF PROSTAGLANDIN E2 (PGE2) AND AMELIORATES PGE2-RELATED URINARY SYMPTOMS.

Hypothesis / aims of study

Excessive production of ProstaglandinE2 (PGE2) induced in the bladder by stretch or inflammation is involved in micturition pain or OAB symptoms; and leads to deterioration of the patient's QOL. Although oral non steroidal anti-inflammatory drugs (NSAIDs) are useful for managing symptoms related to excessive production of PGE2, they have severe adverse side-effects, including GI tract problems or renal failure, and reduce PGE2 excretion in urine due to a decline in kidney production [1.2)]. On the other hand, topical NSAIDs are known to work on target organs through local delivery.

The aim of this study is to evaluate whether NSAID topically applied to the perineum is locally delivered to the lower urinary tract where it can suppress excessive production of PGE2; and whether it ameliorates the symptoms related to excessive production of PGE2 without the adverse side-effects associated with circulating NSAIDs.

Study design, materials and methods

A total of 50 male patients who were to undergo transurethral prostatectomy (TUR-P n=25) or bladder tumor resection (TUR-Bt n=25) were enrolled in this study. Patients were randomly divided into a treated group and an untreated group. 500 mg Difrogenac gel was applied to the perineum twice a day for 1 week after balloon removal. Before the operation, and on the 3rd and 7th day after balloon removal, the amount of PGE2 in urine voided in 24 hours was measured, and the degree of micturition pain was evaluated using a 5 phase visual pain scale. 11 volunteers who did not undergo lower urinary tract surgery (LUTS) topically applied NSAID to evaluate the effect on production of PGE2 derived from the upper urinary tract.

Results

Full results were obtained for 46 eligible patients. There were no differences in urinary PGE2 before treatment among the treated, untreated, and non-LUTS volunteer groups. In the untreated group, urinary PGE2 significantly increased on both the 3rd and 7th day after balloon removal ($p<0.0001$) (Fig.1). On the other hand, in the treated and volunteer groups, urinary PGE2 did not change significantly after surgery or application of NSAID (Fig.1). In the untreated group, the degree of micturition pain was worse on both the 3rd and 7th day after balloon removal ($p<0.0001$) (Fig.2). In the treated group, the degree of micturition pain did not change significantly after surgery (Fig.2). No adverse side-effects associated with the topical application of NSAID were observed, and no patients in the treated group needed other analgesic drugs during treatment.

Interpretation of results

In this study, topical application of NSAID effectively relieved micturition pain induced by transurethral surgery without obvious adverse side-effects. Urinary PGE2 in volunteer non-LUTS patients did not change during topical NSAID treatment. This suggests that very little topical NSAID migrated into the bloodstream from the perineum, since circulating NSAIDs reduce urinary PGE2[1.2)]. The level of urinary PGE2 clearly increased in the untreated group following surgery. On the other hand, urinary PGE2 in the treated group did not change following surgery. Since migration of the topically applied NSAID from the perineum into the bloodstream appears to be very low, we conclude that NSAID topically applied at the perineum is locally delivered to the lower urinary tract where it inhibits excessive PGE2 production.

Concluding message

NSAID topically applied at the perineum may be locally delivered to the lower urinary tract where it inhibits excessive PGE2 production. This may be a useful treatment to manage LUTS without the adverse side effects associated with circulating NSAIDs.

Fig.1. The influence of topical NSAID on urinary PGE2

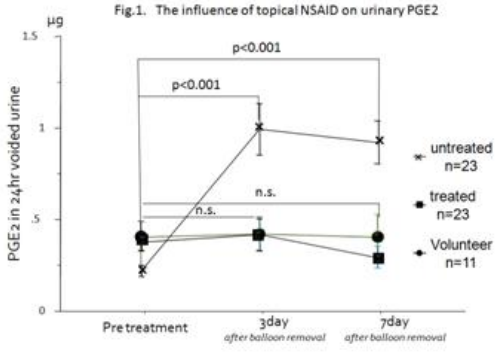
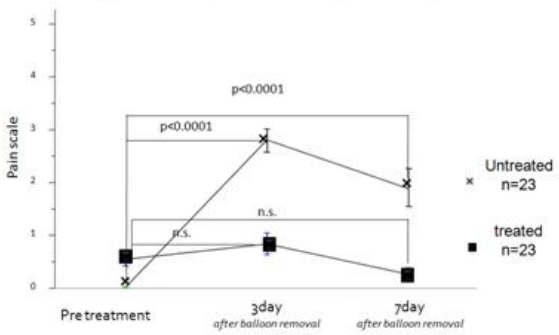


Fig.2. The efficacy of topical NSAID against miction pain



References

1. J Endocrinol Invest:2(2):173-182,1979
2. Eur J Pediatr 41(2):71-76,1983

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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Review board at Nara medical university**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**