bladder and bladder afferent pathways in a diabetic model. We employed HSV type 1 vectors which express a functionally active form of mouse β-NGF.

Methods

NGF expression during latent (10 weeks) infection was examined by ELISA and immunohistochemistry following injection of HSV-NGF expression vectors ($1x10^{6-8}$) into the bladder wall of the adult female SD (250-275 gr) rat with and without streptozotocin (STZ) [75 mg/kg]. Six wk. after STZ-induction (glucose > 350 mg/dl) the animals were injected with nonreplicating, latency promoter driven HSV-NGF and were sacrificed after an additional 4 weeks. Metabolic cages were used to monitor urination frequency and voided volume. Cystometrogram were done at the time of sacrifice and ELISA and immunohistochemistry were performed.

Results

Replication defective vectors containing HSV-1 latency promoter (LAP-2) driving β-NGF gene were able to express NGF in the bladder and DRG at 4 weeks after bladder injection. ELISA analysis confirmed an approximately 4 fold increase of NGF expression in both bladder and L6-S1 DRG.

STZ-treated rats with sham-HSV at 10 wk. had much higher voided volume per micturition (3.69 ± 0.98 ml) [n=3] than control animals (0.55 ± 0.40 ml) ($p<0.001$). However, STZ-induced rats that were injected with HSV-NGF [n=5] had voided volume per micturition of only 2.19 ± 0.55 ml at week-10. STZ-induced animals injected with sham HSV had CMG bladder capacity of 3.20 ± 0.84 while HSV-NGF injected animals had capacity of 1.40 ± 0.69 ml.

Conclusions

NGF gene could be expressed in the bladder and bladder afferent pathways using a nonreplicating latency promoter HSV vectors that is well tolerated. This is the first demonstration that NGF gene therapy can revert the STZ-induced diabetic bladder changes. This technique of gene transfer might be useful for treating patients with diabetic cystopathy.

20

RD Brierly, RG Hindley, DM Harding, PJ Thomas.

The Royal Sussex County Hospital, Brighton, United Kingdom.

MORPHOLOGICAL CHANGES ASSOCIATED WITH IMPAIRED DETRUSOR CONTRACTILITY.

Aims of study

Elbadawi *et al* [1] first described abnormalities, using qualitative electron microscopic study of detrusor muscle biopsies in patients with impaired contractility in the stable unobstructed bladder compared with normal. These ultrastructural features were later refined [2]. Patients with impaired contractility were found to have specific morphological features termed the degeneration pattern. That is the presence of disruptive muscle cell profiles in at least 50% of randomly studied fields. Disruptive degeneration features include sarcoplasmic vacuolation, sequestration or blebbing, cell shrivelling and fragmentation as well as the presence of cell debris in intercellular spaces.

A second described pattern is a sub-group of patients, associated with a history of chronic bladder overdistension termed the hyperelastosis pattern, that is localised areas of indistinct muscle fascicle arrangement with abundant elastic fibres intermingled with separating and disrupting collagen fibres in wide intercellular spaces.
This study was aimed to assess whether impaired bladder contractility is associated with morphological differences on electron microscopy of detrusor muscle when compared with age matched controls.

Methods:

1) Impaired contractility group
23 patients were studied (18 male and 2 female, mean age 64)

•Residual volumes consistently >300mls

•All patients reliant on CISC or IDC

•Graded as weak or very weak on Shafer's nomogram

2) Control group
7 Patients studied (6 male and 1 female, mean age 57)

•Asymptomatic normal voiders

•Residual volumes consistently <50mls

Two bladder biopsies were obtained from all patients endoscopically using the cold-cup technique. Specimens were then processed for electron microscopy by standard methods. The ultrastructural arrangement of each specimen was examined in detail and documented photographically.

Results:
The criteria of the degeneration pattern was fulfilled in all of the biopsies from patients in the impaired contractility group.
Six of the patients (5 male and 1 female, mean age 70) from the impaired contractility group were found to have localised areas of the hyperelastosis pattern in addition. All of these patients had a history of large bladder residual volumes in excess of 1500ml. All of these patients had a past history of chronic urinary retention and four of the males had received previous bladder neck surgery, the remaining male and female had idiopathic aetiology.
The above morphological patterns were not seen in any of the control group.

Conclusion:
Our findings would support the degeneration pattern as the structural correlate of detrusor hypocontractility and suggests that the hyperelastosis pattern is a structural correlate of previous chronic bladder overdistension and may identify a sub-group of patients with impaired detrusor contractility.
We have demonstrated that by using electron microscopy, there are reproducible distinct morphological patterns seen on detrusor biopsies, which correlate with impaired detrusor contractility.

References:
[1] J Urol 1993; **150**:1657-1667.
[2] J Urol 1997; **157**:1783-1801.