140

Intravesical treatment of polysaccharide alginate/collagen gel in a swine model of ketamine cystitis

Meng E[1], Fan G[2], Chang S[3], Cherng J[4], Wu S[5]

[1] Division of Urology, Department of Surgery, Tri-Service General Hospital, Taipei, Taiwan, ROC.,
[2] Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, ROC.,
[3] School of Dentistry, National Yang-Ming University, Taipei, Taiwan, ROC.,
[4] Department and Graduate Institute of Biology and Anatomy, Taipei, Taiwan, ROC.,
[5] Division of Urology, Department of Surgery, Tri-Service General Hospital, Taipei, Taiwan, ROC.

ABSTRACT

Since the pathophysiology of ketamine-induced cystitis is still unclear, no effective treatments are currently available. The aim of this study was to develop a ketamine-induced cystitis (KC) swine model to evaluate the intravesical polysaccharide alginate/collagen gel treatment. In this study, we used the swine, which shares greater similarities with a human than a mouse or a rat does, as a model for studying human diseases. The female Lanyu swine were injected ketamine to induce cystitis. The bladder function was characterized by cystoscopy, urodynamic, histological evaluations and PCR-array. The swine were distributed into three groups: (1) normal saline injection 12 weeks then treated with normal saline(C-C group); (2) ketamine injection 12 weeks then treated with normal saline(K-C group); (3) ketamine injection 12 weeks then treated with polysaccharide alginate/collagen(K-T group). The swine bladders were irrigated with polysaccharide alginate/collagen gel or saline once a week for 4 weeks. After 12 weeks of ketamine injection, cystoscopy revealed remarkable engorged vessels in the ketamine-treated swine bladder. The urodynamic study showed that the inter-contraction interval in ketamine-treated swine were lower than normal saline-treated swine. The histological exam demonstrated that inflammatory cells infiltrated in the bladder wall of K-C group but not in C-C and K-T group. PCR-array data showed that some genes were regeneration in K-T groups. Swine bladder may be affected by long-term ketamine administration as the human bladder. Polysaccharide alginate/collagen may have potential to recover the bladder function of KC patients. We have established the first swine ketamine-induced cystitis model which may help us better understand the pathophysiology of KC and intravesical polysaccharide alginate/collagen treatment may have potential to treat ketamine-induced cystitis .

AIM

The aim of this study was to develop a ketamine-induced cystitis swine model to evaluate the intravesical polysaccharide alginate/collagen gel treatment.

MATERIALS and METHODS

The swine were injected normal saline or ketamine daily for 12 weeks, then the bladder was irrigated with 50 mL of polysaccharide alginate/collagen gel or saline once a week for 4 weeks. Urodynamic study and cystoscopy were performed after ketamine administration for 12 weeks and after 4 weeks of alginate/collagen gel treatment. The swine were sacrificed at the end of experiments, and the bladder sample was analyzed with H-E stain, masson trichrome stain. We also used RT 2 Profiler™ PCR-array as validation in a pig extracellular matrix and adhesion molecules study to assay the expression of a functionally diverse set of 84 genes.

RESULTS

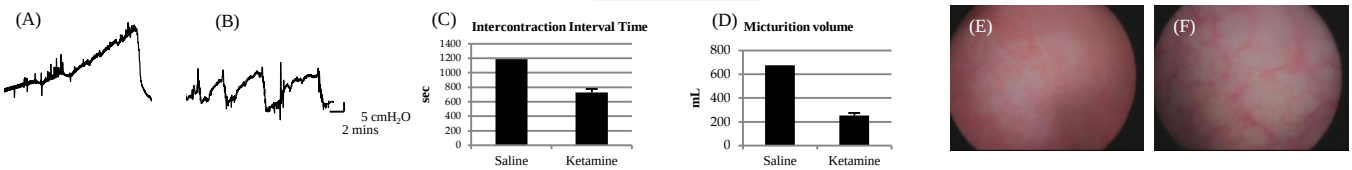

Figure 1. Intravesical pressure of saline(A) and ketamine(B) injected swine show increased frequency after 12 weeks of ketamine injection. Inter-contraction interval and micturition volume decreased in ketamine injected swine(C, D) . Endoscopy of swine urinary bladder after 12 weeks administered with saline(E) and ketamine(F) revealed remarkable engorged vessels in the ketamine-treated swine bladder.

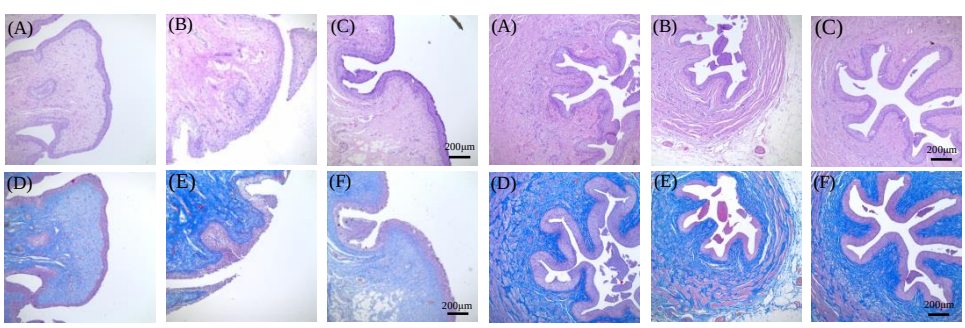

Figure 2. The bladder H-E stain and masson trichrome stain results of C-C group(A, B), K-C group(C, D) and K-T group(E, F) show that inflammatory cells infiltrated in the bladder wall of K-C group but not in C-C and K-T group. The stratification of urothelium of K-T group was similar to C-C group.

Figure 3. The ureter H-E stain and masson trichrome stain results of C-C group(A, B), K-C group(C, D) and K-T group(E, F) show that tissue morphology of K-C groups was different to the other groups.

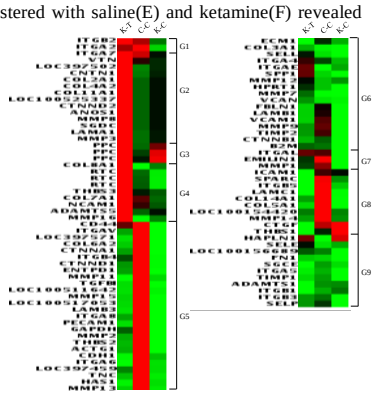

Figure 4. Total bladder mRNA transcript levels of 84 genes were measured and presented as a heat map representing the relative value of the gene expression across all samples. G1–G9 denotes expression distinct groups of genes

CONCLUSION

We have established the first swine KC model which may help us better understand the pathophysiology of ketamine cystitis. Swine bladder can be affected by long-term ketamine administration as the human bladder. We also found that some gene mRNA expression may regenerate after intravesical alginate/collagen treatment showing that extracellular matrix may have potential to treat ketamine cystitis.