

STUDIES ON REGENERATED RABBIT BLADDER TISSUE USING SMALL INTESTINAL SUBMUCOSA

Hypothesis / aims of study

Conventional enterocystoplasty is always associated with a variety of complications, which in turn stimulated the development of alternative methods for bladder augmentation. The need to find an alternative to the use of bowel for urinary reconstruction has renewed research interests involving bladder regeneration. Small-intestinal submucosa (SIS) is an acellular, nonimmunogenic, biodegradable, xenogeneic, collagen-based material that is derived from the submucosa layer of porcine small intestine. SIS has demonstrated regenerative capacities in multiple organ systems, including the aorta, vena cava, ligaments, tendons, abdominal wall, and skin. And SIS has also demonstrated long-term reliable regenerative results in the rat and canine bladder-augmentation models.

The aim of this study was to investigate the functional and histological characteristics of small intestine submucosa (SIS) as bladder wall replacement in a rabbit-augmentation model.

Study design, materials and methods

Eighteen New Zealand male rabbits (weight 2.5-3.5kg) will be used. All rabbits will be divided into 3 groups with 6 rabbits in each group. All rabbits firstly will receive urodynamic tests to detect the bladder capacity and DLPP. Then they will receive ventral bladder section and a single layer of SIS (COOK[®], 1×2cm) will be sewn to bladder with 5/0 vicryl suture material in a watertight manner. Then three groups of rabbits will receive an urodynamic test in 4, 12 and 24 weeks after the operation respectively. Then after the tests they will be euthanized with an overdose of pentobarbital and perivesical fat will be removed together with bladder. The 5µm preparations, taken from the SIS-regenerative bladder tissues, will be stained with haematoxylin-eosin, monoclonal antibodies to smooth muscle α -actin for histologic and immunocytochemical analyses of the structure of regenerated bladder, compared to the normal bladder. In the other side, SIS-regenerated bladder strips (10×3×3 mm) will be obtained and received contractility tests in vitro for evaluating the contractility of SIS-regenerated bladder muscle.

Results

Histologically, the SIS-regenerated bladders of 24 weeks group resembled normal bladder in that all 3 layers (mucosa with submucosa, smooth muscle, serosa) were present. While in the 4 weeks group, the surface of the graft material was covered by regenerated bladder tissue. And the material hadn't been degraded completely yet. Stone formation on the material was seen in the 4 weeks group.

In vitro detrusor strip study, there were no significant difference in autorhythmicity and contractility between regenerated (frequency: $4.35 \pm 1.25 \text{ min}^{-1}$; amplitude: $0.5 \pm 0.25 \text{ g}$) and normal (frequency: $3.64 \pm 0.98 \text{ min}^{-1}$; amplitude: $0.69 \pm 0.09 \text{ g}$) tissue in 24 weeks group ($p > 0.05$). And the strips in 12 weeks group decreased more significantly in autorhythmicity and contractility of regenerated (frequency: $2.88 \pm 0.49 \text{ min}^{-1}$; amplitude: $0.13 \pm 0.014 \text{ g}$) tissue than normal frequency: $4.8 \pm 1.2 \text{ min}^{-1}$; amplitude: $0.47 \pm 0.083 \text{ g}$) ($p < 0.05$). While in the 4 weeks group, it could be only seen tiny waver in regenerated tissue which couldn't be obtained comparable date.

Urodynamic test showed that, postoperatively, DLPP of all the groups had slightly decreased mean DLPP; however, this was not statistically different from their preoperative values. Mean bladder capacity of 4 weeks group ($26.1 \pm 4.75 \text{ ml}$) decreased more significantly than preoperative values ($40.3 \pm 7.63 \text{ ml}$) of this group ($p < 0.05$). While, in the 6 weeks group the bladder capacity had increased after operation and this was statistically different from their preoperative values.

Interpretation of results

In this study, there were no significant differences in the parameters of vitro detrusor strip test in 24 weeks group between regenerated tissue and normal. These results indicate that the detrusor had completely regenerated with similar normal contractility in 24 weeks. The result that bladder capacity decreased in 4 weeks group after operation could due to the stone which formed in the bladder at that time. And no stone was seen in other two groups indicated that the stone might be temporary and couldn't made any effect to the further results.

Concluding message

The results obtained from this study indicate that (1) Detrusor could regenerate with similar normal function by the help of SIS. (2) The regenerated bladder had lower DLPP and larger capacity. (3) SIS seems to be a viable alternative to the use of intestine in the reconstruction of the urinary system but advanced and more detailed investigations should be carried out.

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Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	Ethical committee of China Rehabilitation Research Center