

RECONSTRUCTIVE UROLOGY

Growth of Bone Marrow Stromal Cells on Small Intestinal Submucosa: An Alternative Cell Source for Tissue Engineered Bladder

Zhang Y, Lin HK, Frimberger D, Epstein RB, Kropp BP

Department of Urology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

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Objective: To assess the potential use of bone marrow stromal cell (BMSC)-seeded biodegradable scaffold for bladder regeneration in a canine model, by characterizing BMSCs and comparing them to bladder smooth muscle cells (SMCs) by immunohistochemistry, growth capability, and contractility.

Materials and Methods: Bone marrow was taken by direct needle aspiration from the femurs of five beagle dogs for the in vitro study. Mononuclear cells were isolated by Ficoll-Paque density gradient centrifugation and cultivated in medium 199 with 10% fetal bovine serum. BMSCs were characterized by cell proliferation, in vitro contractility, immunohistochemical analysis, and the growth pattern on small intestinal submucosa (SIS) scaffolds compared to bladder SMC cultures from the same dogs. Another six dogs had a hemicycstectomy and bladder augmentation with BMSC-seeded (two), bladder cells including urothelial cells plus SMC-seeded SIS (two) and unseeded SIS scaffolds (two). The six dogs were followed for 10 weeks after augmentation.

Results: In vitro BMSCs had a significant contractile response to calcium-ionophore, with a mean (sem) 36 (2) %, relative contraction ($P < 0.01$), which was similar to bladder SMCs but markedly different from fibroblasts. BMSCs also expressed alpha-smooth muscle actin by immunohistochemical staining and Western blotting, but did not express desmin or myosin. In vivo, both BMSC-seeded and bladder cell-seeded SIS grafts had solid smooth-muscle bundle formation throughout the graft.

Conclusions: BMSCs had a similar cell proliferation, histological appearance and contractile phenotype as primary cultured bladder SMCs. SIS supported three-dimensional growth of BMSCs in vitro, and BMSC-seeded SIS scaffold promoted bladder regeneration in a canine model. BMSCs may serve as an alternative cell source in urological tissue engineering.

Editorial Comment

During recent years, biodegradable scaffolds demonstrated a good source for bladder wall regeneration. Some performed better than others, such as polyglycolic acid and other produced scaffolds, in comparison to small intestine submucosa (SIS) or organ specific acellular matrix (bladder acellular matrix graft (BAMG)) which demonstrated the potential to support tissue regeneration. All have in common that the cells migrate from the host to the center of the scaffold. This might be too slow in that fibrotic changes can happen in the center of the implant before the migration line reaches the center. The result is a scar without function or even worse, shrinking tissue dependent.

To avoid this effect, cell seeding prior to the implantation gives faster recovery, function and reduction of possible scarring. Zhang et al. differentiated bone marrow stromal cells (BMSC's) into smooth muscle cells. For comparison, they cultured bladder smooth muscle cells (SMC's) of the same animal. In addition to an almost equal histological outcome, the intensity for α -smooth muscle actin was brighter in the differentiated BMSC's with a better contractility in Ca^{2+} -ionophore conditions. Both types of cells grew on and into the SIS scaffold in several layers. Finally augmented to the bladder, cell-matrix implants demonstrated bladder wall regeneration, which was better for BMSC differentiated cells throughout the complete SIS.

The comparison between BMSC and bladder SMC nicely demonstrates the advantage of bone marrow-derived stromal cells, which do have the potency to differentiate myogenically. The seeded scaffold regenerates faster in comparison to the unseeded, but the results are preliminary because each in-vivo group consists of just two animals. The disadvantage is the requirement of 10% fetal bovine serum, which is not in accordance with the principles of Good Medical Practices (GMP) and currently makes impossible to introduce this technique into the clinic.

Reference

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*Dr. Karl-Dietrich Sievert,
Dr. Gerhard Feil, & Dr. Arnulf Stenzl
Department of Urology
Eberhard-Karls-University Tuebingen
Tuebingen, Germany*

Cyanoacrylic Glue: A Minimally Invasive Nonsurgical First Line Approach for the Treatment of Some Urinary Fistulas

Muto G, D'Urso L, Castelli E, Formiconi A, Bardari F
Department of Urology, S. Giovanni Bosco Hospital, Turin, Italy
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Purpose: We evaluated the adaptability and the efficacy of cyanoacrylic glue for the conservative treatment of urinary fistulas of different etiologies using an endoscopic, percutaneous or endovaginal approach.

Materials and Methods: From May 1998 to July 2004, 13 patients with long lasting iatrogenic and/or inflammatory urinary fistulas were treated conservatively with endoscopic, percutaneous or endovaginal application of 1 to 3 cc of cyanoacrylic glue.

Results: The complication rate in this cohort of 13 patients was low. Occlusion therapy failed in 2 genitourinary fistulas, which were wider (diameter greater than 1 cm) and short. In the remaining 11 cases, urinary fistulas were successfully sealed and at a median followup of 35 months, no relapses were observed.

Conclusions: Cyanoacrylic glue is suitable for endoscopic, percutaneous and endovaginal use. This occlusion therapy represents a safe and minimally invasive approach that might be offered as a first line option for the treatment of urinary fistulas, especially narrow and long tract fistulas.

Editorial Comment

After failed conservative therapy (at least by two months catheterization), Muto et al. treated iatrogenic and/or inflammatory urinary fistulas with the use of cyanoacrylic glue. The established therapeutic approach in all reported cases (anastomotic neovesicoileal-, neovesicourethral-, anastomotic neovesivocutaneos-, prostatoperineal-, vesicosigmoid and vesicovaginal-fistula) is open surgery. In times where economic aspects play an increasing role in medicine, new minimal invasive approaches with decreased hospitalization and surgical time needs to be evaluated. In recent times, new sealants became available and modified endoscopic techniques promised a satisfying result in fistula repair. Independent of fistula location and diameters (from 0.5 – 2.0 cm), 13 patients were treated with the use of cyanoacrylic glue. After a median follow-up of 35 months, 11

patients (85%) had successful outcomes. Treatment failed in 2 patients with short fistulas larger than 1.5 and 2.0 cm in diameter. Occlusion therapy represents a safe and minimally invasive approach that may be offered as a first option for fistulas of the urinary tract with a diameter less than 1.5 cm.

Those iatrogenic fistulas might be prevented by the use of Gelatine Matrix Haemostatic Sealant (GMHS). GMHS with thrombin is used in surgical procedures to adjunct haemostasis when control of bleeding by conventional procedures is ineffective or impractical. In addition, the stable matrix expands up to 20% in volume when in contact with blood, resulting in a closure of the access tract and compressing the surrounding tissue. Recently, we used this sealant very successful close to the vesicourethral anastomosis (radical prostatectomy) or the neovesicourethral anastomosis (cystoprostatectomy) as an additional sealant after PCNL (1) and mini-PCNL (2). This modified technique might help to prevent iatrogenic induced epithelialized urinary fistula. Muto et al. report offers a new choice to treat occurred ones less invasive.

References

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*Dr. Udo Nagele, Dr. Karl-Dietrich Sievert,
Dr. Markus Kuczyk & Dr. Arnulf Stenzl
Department of Urology
Eberhard-Karls-University Tuebingen
Tuebingen, Germany*

UROLOGICAL ONCOLOGY

Predicting Recurrence and Progression in Individual Patients with Stage Ta T1 Bladder Cancer Using EORTC Risk Tables: A Combined Analysis of 2596 Patients from Seven EORTC Trials

Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffouix C, Denis L, Newling DW, Kurth K
EORTC Data Center, Brussels, Belgium
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Objectives: To provide tables that allow urologists to easily calculate a superficial bladder cancer patient's short- and long-term risks of recurrence and progression after transurethral resection.

Methods: A combined analysis was carried out of individual patient data from 2596 superficial bladder cancer patients included in seven European Organization for Research and Treatment of Cancer trials.

Results: A simple scoring system was derived based on six clinical and pathological factors: number of tumors, tumor size, prior recurrence rate, T category, carcinoma in situ, and grade. The probabilities of recurrence and progression at one year ranged from 15% to 61% and from less than 1% to 17%, respectively. At five years, the probabilities of recurrence and progression ranged from 31% to 78% and from less than 1% to 45%.

Conclusions: With these probabilities, the urologist can discuss the different options with the patient to determine the most appropriate treatment and frequency of follow-up.