

## AUTOLOGOUS ADIPOSE STEM CELLS IN TREATMENT OF FEMALE STRESS URINARY INCONTINENCE

### Hypothesis / aims of study

The aim of the study was to find out if transurethral injections of autologous adipose stem cells (ASCs) are an effective and a safe treatment for female stress urinary incontinence (SUI). The primary end point was cough test to objectively measure the effect of the treatment. Validated questionnaires were used for determining the subjective cure rate.

### Study design, materials and methods

Five SUI patients were treated with autologous adipose stem cells combined with bovine collagen gel (Contigen™) and saline solution between February 2010 and January 2011. The subcutaneous fat (0,3-0,5dl per patient) from lower abdomen was collected under local anaesthesia. Fat was collected from six patients but because of bacterial contamination the treatment was refrained from one patient. The ASCs were isolated and augmented for three weeks in a GMP-laboratory. Mixture of ASCs (altogether 10x10E6/patient) and collagen (Contigen™) was injected transurethrally via cystoscope. The injections were placed just under mucosa about 1,5cm distal from the urethral neck at 3 and 9 o'clock, injected volume being 2,4-4ml per patient. Additional injections of ASCs mixed with saline solution were done slightly more distal in order to bring more stem cells in contact with urethral smooth muscle, injected volume being 2ml per patient. The patients are being followed at 3, 6 and 12 months after the injections by gynaecological examination, ultrasonography, cough test, 48h pad test, standardized questionnaires and urodynamic evaluations.

### Results

So far four patients have reached six month follow-up. With the exception of small haematomas there were no adverse events from the adipose tissue collection. There were neither any complications (urinary retention, haematuria, urinary infection) after the transurethral injections. At six months, one out of four patients displayed a negative cough test. There was some subjective improvement with all four patients according to the Urinary Incontinence Severity Score (UISS), the Incontinence Impact Questionnaire-Short Form (IIQ-7), the Urogenital Distress Inventory-Short Form (UDI-6), and a visual analogue scale (VAS), but the results are somewhat conflicting and so far three out of four patients have been scheduled for operative treatment.

### Interpretation of results

Our preliminary results of ASCs to treat female stress urinary incontinence were not as effective as hypothesized according to the previous clinical cell therapy studies<sup>1,2</sup>. That's why the study has been stopped at this point. There can be several reasons why the therapeutic effect of the ASC therapy was vague. The bovine collagen gel (Contigen™) may not be the ideal carrier for the ASCs. Therefore injected cells may not be able to stay in contact with the patient's muscle cells long enough to have time to differentiate into muscle cells to form a better sphincter around the urethra. Three of the five patients had a recurrent SUI that is often challenging for operative treatment as well. At this point we are looking for better bioabsorbable injectable material for ASCs and an ideal technique for transurethral injections to enhance the strength of the sphincter muscle of urethra to effectively treat female SUI.

### Concluding message

Autologous adipose stem cells combined with bovine collagen and saline solution are not a very effective treatment for female stress urinary incontinence with this method. We need more studies to find a better carrier and the ideal technique for the transurethral injections. So far the treatment with ASCs has proven safe and well tolerated.

### References

1. Mitterberger M, Pinggera G-M, Marksteiner R, Margreiter E, Fussenegger M, Frauscher F, Ulmer H, Hering S, Bartsch G, Strasser H: Adult stem cell therapy of female stress urinary incontinence. *Eur Urol* 2008;53:169-75
2. Carr LK, Steele D, Steele S, Wagner D, Pruchnic R, Jankowski R, Erickson J, Huard J, Chancellor MB: 1-year follow-up of autologous muscle-derived stem cell injection pilot study to treat stress urinary incontinence. *Int Urogynecol J* 2008;19:881-3

<b>Specify source of funding or grant</b>	<b>NONE</b>
<b>Is this a clinical trial?</b>	<b>Yes</b>
<b>Is this study registered in a public clinical trials registry?</b>	<b>No</b>
<b>Is this a Randomised Controlled Trial (RCT)?</b>	<b>No</b>
<b>What were the subjects in the study?</b>	<b>HUMAN</b>
<b>Was this study approved by an ethics committee?</b>	<b>Yes</b>
<b>Specify Name of Ethics Committee</b>	<b>Ethical Committee of Pirkanmaa Hospital District</b>
<b>Was the Declaration of Helsinki followed?</b>	<b>Yes</b>
<b>Was informed consent obtained from the patients?</b>	<b>Yes</b>

