

THERAPY OF REFRACTORY POSTOPERATIVE URINARY STRESS INCONTINENCE BY THE USE OF AUTOLOGOUS SKELETAL MUSCLE- DERIVED CELLS (MDC)

Hypothesis/Aim of study:

Urinary stress incontinence (USI) caused by morphological injury of the external urethral sphincter is refractory to conservative treatment. According to §4a of the German Pharmaceutical Law (AMG) we treated patients suffering from postoperative refractory grade III urinary stress incontinence by transplantation of MDC in order to possibly reconstruct the sphincter morphology and function. Patients were sent to our clinic from all parts of Germany.

Material and Methods:

In general or local anaesthesia muscle tissue is extracted from the deltoid muscle (sample size 5x5mm, 2 samples/patient). The muscle tissue is converted into a primary cell culture separating individual cells and expanding them. Prior to the transplantation MDC are stored in physiological soda solution. Under visual guidance the cells are endoscopically injected into and around the lesion of the external sphincter.

Results:

222 male patients aged 70 years (range: 56-81) from 32 different hospitals in Germany were included. 60% (132/222) of the patients were followed-up for at least 12 months after MDC transplantation- the time span necessary for sufficient evaluation of the transplantation process. The average time since iatrogenic sphincter injury was 43 months (range: 12-192).

After a medium of 59 days (range: 16-122) following the muscle biopsy transplantation of MDC was performed. 11.18×10^6 (range: $0.21-29.23 \times 10^6$) of MDC were transplanted.

11.3 % (range: 9.5-13.1%) of these cells are identified immunocytochemically as satellite cells (positive for MyoD1, α -sarcomeric actin, α -smooth-muscle actin).

Reversible adverse events grade I were observed in 11% of the patients (15/132).

After a minimum follow-up of 12 months (range: 12-61) 18 patients (13.6%) were completely continent, 51 patients (38.6%) showed improvement from grade III urinary stress incontinence to grade I (less than 100ml/24h uncontrolled urine loss).

The treatment effect can be observed 4.7 months (range: 2-9) after transplantation of MDC and remains stable during follow-up. 63/132 (48%) patients have no change regarding grade III incontinence. Control cystoscopy showed a morphologically intact external sphincter in 15% (20/63) of the patients despite lacking improvement of USI.

Interpretation of results:

The transplantation of MDC for the repair of iatrogenic damage of the external urinary sphincter and consecutive grade III urinary stress incontinence is a safe procedure. In 52% (69/132) of the patients this minimally invasive method is efficient in distinctively reducing incontinence or even healing it.

Concluding message:

Apart from the efficacy of the minimally invasive procedure disadvantages are the expenditure of time between treatment and efficacy of about 7 months, the cost situation which until today is at our own expense exclusively, and the restrictions resulting from §4a AMG (German Pharmaceutical Law) prohibiting us the initiation of GCP- conform clinical trials.

Specify source of funding or grant	None
Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	No
This study did not require ethics committee approval because	ethical approval not required due to performance of the study according to §4 German Pharmaceutical Law
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes