

THE POTENTIAL ROLE OF STEM CELLS IN THE TREATMENT OF FECAL INCONTINENCE FOLLOWING POSTERIOR SAGITTAL ANORECTOPLASTY OPERATION

Hypothesis / aims of study

Surgical repair of the anal sphincter is the main treatment approach for treating fecal incontinence caused by anatomical defects. Currently, the most exciting and promising incontinence research is focused on regenerative repair of damaged rhabdosphincter with stem cell therapy. Mesenchymal Stem Cells (MSC) injection may represent a new attractive treatment option for anal sphincter lesions [1]

The aim of this study is to investigate the potential therapeutic effects of local MSC injection in children presenting with fecal incontinence (FI) after posterior sagittal anorectoplasty (PSARP) operation for high imperforate anus.

Study design, materials and methods

Study Design: preliminary, non-randomized single group assignment, open Label, interventional study. Children with FI following PSARP surgery for repair of high imperforate anus were included. Children having associated rectal prolapse, rectocele, or any neurological abnormalities or sacral deformities were excluded.

After taking history and confirming fecal incontinence based on the Wexner Continence Grading Score [2], all subjects underwent electromyography (EMG) and MRI pelvic floor muscle testing.

Ten ml bone marrow sample was extracted from the patient's iliac crest, using a heparinized syringe, under general anesthesia and in a suitable clean operation room. The method of isolation of MSC from bone marrow was carried out using the Ficoll-Paque technique for the isolation of mononucleated cells followed by the separation of MSC. Finally, the cells were re-suspended and counted using a hemocytometer. Mononucleated cells were cultured and incubated at 37°C in an atmosphere of 95% relative humidity and 5% CO₂.

A single dose of 1.2 ml MSC was divided into 12 parts of 0.1ml of MSC, then injected into the anal sphincter all around in 12 injection sites according to the clock meridian under general anesthesia and direct ultrasound guide (Figure 1 & 2)

Anal sphincter EMG (for external anal sphincter, puborectalis and levator ani muscles), was performed using disposable concentric needle electrode. Activity was recorded during muscle relaxation and contraction. The external anal sphincter muscle was tested in the four quadrants of the anal opening (sites 3, 6, 9 and 12 o'clock).

All patients were followed up clinically using Wexner score for one year. Post injection anal EMG and MRI pelvic floor muscle were performed at 1, 3 and 6 months post-injection. Data were compared with pre injection ones.

Results

Twelve boys were consecutively enrolled in the study. Their mean age was 7.3 years (range 4-11 years). All of them had EMG and MRI evidence of a muscular defect of the external anal sphincter of different degrees. They had also history of failed conservative treatment.

Injection was very well tolerated by all patients with no evidence of immediate or delayed side effects. The average injection time was 11 minutes for each patient.

There was a highly significant reduction in incontinence scores with improved symptoms over the first six months study period (Wexner score decreased by a mean of 15.52 units, $P < 0.05$). Unfortunately, scores deteriorated with time and had nearly returned to baseline by the end of one year (figure 3 & 4).

EMG activity of pelvic floor muscles was measured as the mean amplitude/turn and mean number of turns/second during maximum squeezing. No significant change in EMG activity could be detected between pre-and 1, 3 or 6 months post injections. MRI pelvic floor muscles showed also no significant change in the thickness of any anal sphincter component over the course of the study.

Interpretation of results

In our study, the overall results of our approach are not satisfactory. The markedly but un-sustained improvement in clinical scores couldn't be explained. We were unable also to demonstrate any sustained physiological change detected by EMG or anatomical changes detected by MRI, to account for the improvements we observed clinically.

We hypothesized that the injected MSCs couldn't integrate into the damaged external sphincter and were unable to improve its functional integrity but it is still able to improve the clinical symptoms for short period may be due to its effect as bulking agent.

Sarveazad et al [3] conducted a randomized double-blind clinical trial on patients with sphincter defects to investigate the therapeutic effect of injecting stem cells derived from human adipose tissue (hADSCs) into each end of the muscle defect during the repair surgery. Two months later, they followed up patients and concluded that injection of hADSCs during repair surgery may cause replacement of fibrous tissue, which acts as a mechanical support to muscle tissue with contractile function. Although in their study only short term follow up was performed, it may give us another clue for the success of stem cell injection. Early timing of injection or even during the surgery itself would give better results.

Our study does have limitations: The lack of randomized control group (using sham injection, of saline for example) which would exclude any placebo effect and also help to investigate the effect of needling and injection alone on the anal tissues.

The number of enrolled patients is relatively small. There is a need for larger sample of patients, with different degrees of sphincter muscle defects, in order to reach significance.

Concluding message

Many questions are still in need to be answered before stem cell therapy can be introduced into routine surgical practice for fecal incontinence.

Fig 1: U/S of anal canal during injection



Fig 2: U/S after injection

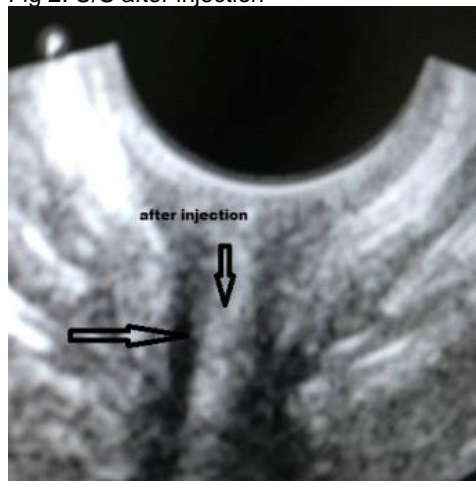


Fig 3: Clinical data over the time course of the study

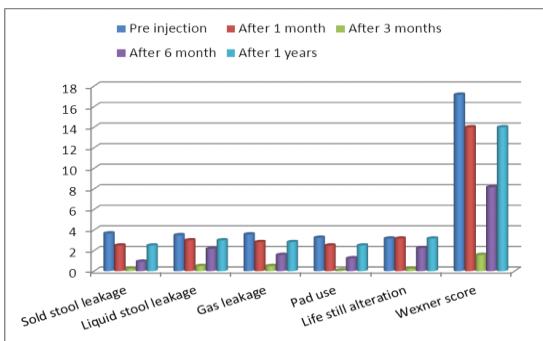
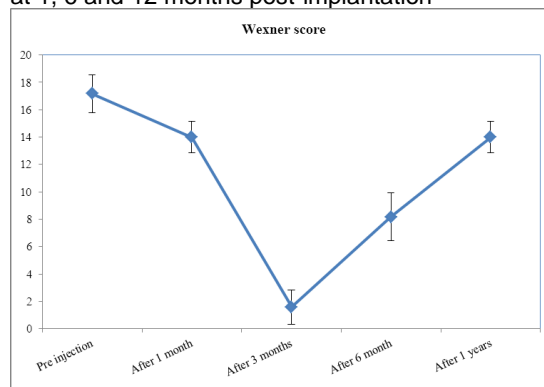


Fig 4: Change in Wexner incontinence score in 12 boys' pre MSC and at 1, 6 and 12 months post-implantation



References

1. Lane, F. L., & Jacobs, S. (2012). Stem cells in gynecology. American journal of obstetrics and gynecology, 207(3), 149-156.
2. Jorge JM, Wexner SD.(1993) Etiology and management of fecal incontinence. Dis Colon Rectum ;36:77-97
3. 4. Sarveazad A et al, (2017): A new method for treating fecal incontinence by implanting stem cells derived from human adipose tissue: preliminary findings of a randomized double-blind clinical trial. Stem Cell Research & Therapy 8:40

Disclosures

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