

# **Autologous Stem Cell Transplantation by lumbar puncture:**

## **A safety Follow-up in 350 Patients**

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## **Abstract**

### ***Background***

Autologous stem cells show promise in preclinical animal models as a cell transplantation therapy for repair of the injured spinal cord, to supplement neural cells in Parkinson, Multiple Sclerosis, Cerebral Palsy and Stroke patients . The procedure of first choice to implant stem cells is lumbar puncture. This procedure is safe and minimal invasive. This paper summarizes the experiences with autologous stem cell therapy and reports the results of 350 lumbar punctures used to inject autologous stem cells into the intrathecal space.

### ***Methods and Results***

A short review of the recent literature looking at the aspect side effects and safety and an oversight of the side effects, reported by post treatment surveillance of patients from Xcell-center Germany. Xcell-center evaluates the side effects of a transplantation with autologous stem cells, using a standard Post Treatment Survey. In this paper, 350 patients with a lumbar puncture as procedure for delivery of the stem cells is reviewed for side effects, using the results of the Post Treatment Surveys. The results of these patients are compared with the side effects after lumbar puncture, reported in literature.

### ***Conclusions***

Within Xcell-center, The incidence of Post Dural Puncture Headache is estimated as low as 3,7% (13 cases out of 350 patients). There were no reported side effects concerning fever, skin rashes, shock or tachycardia. Therefore, the transplantation of autologous stem cells seems to be safe and the lumbar puncture is a safe and non-invasive procedure to inject the stem cells into the intrathecal space. The Post Treatment Survey is a good quality instrument to monitor the safety of the procedure.

### **Key Words**

Autologous stem cells; lumbar puncture; therapy, safety;

## **Introduction**

Lumbar puncture is a frequently performed procedure for diagnosis and therapy delivery<sup>1</sup>. Headache is a common sequela of this procedure irrespective of the indication, although the frequency is less with spinal procedures where fluid is injected and not removed<sup>2</sup>. In general about one third of patients develop headaches after a lumbar puncture procedure<sup>3</sup>. Headache after lumbar puncture occurs more often in young adults<sup>4</sup>. On the other hand, complaints are reported less often after lumbar puncture procedure in young children<sup>5</sup>. Within Xcell-center, lumbar puncture is one of the most often used procedures to inject autologous stem cells into the spinal cavity. In this article, we evaluated the side effect forms of patients treated by Xcell-center using lumbar puncture as therapy procedure and compare these results with literature. In literature, autologous stem cell delivery is safe<sup>6-8</sup> and the only side effects, mentioned are related by the procedure used to inject the stem cells into the target area<sup>9</sup>.

Looking at the science of transplantation and rejection of tissue and blood from blood transfusions, a broad range of complaints can be expected. Because of the use of autologous stem cells and the fact that no eradication of own blood cells take place before stem cell transplantation, there is a very low risk for engraftment syndrome<sup>10,11</sup>. Complaints of rejection are fever, restlessness and skin rashes<sup>12</sup>. One serious risk of lumbar puncture and the injection of fluid components in the intrathecal space is infection. These general and often aspecific symptoms must be monitored during the first days to exclude serious complications.

## **Methods**

Within Xcell-center, all the patients treated with stem cells are followed to detect unexpected side effects. To report side effects, Xcell-center uses the Post Treatment Survey consisting of a first day side effect form (first day of the stem cell delivery), a 10 days side effect form (This take place in the third week after stem cell delivery) and a 3 months evaluation form (asking for long term side effects and first effects of the treatment).



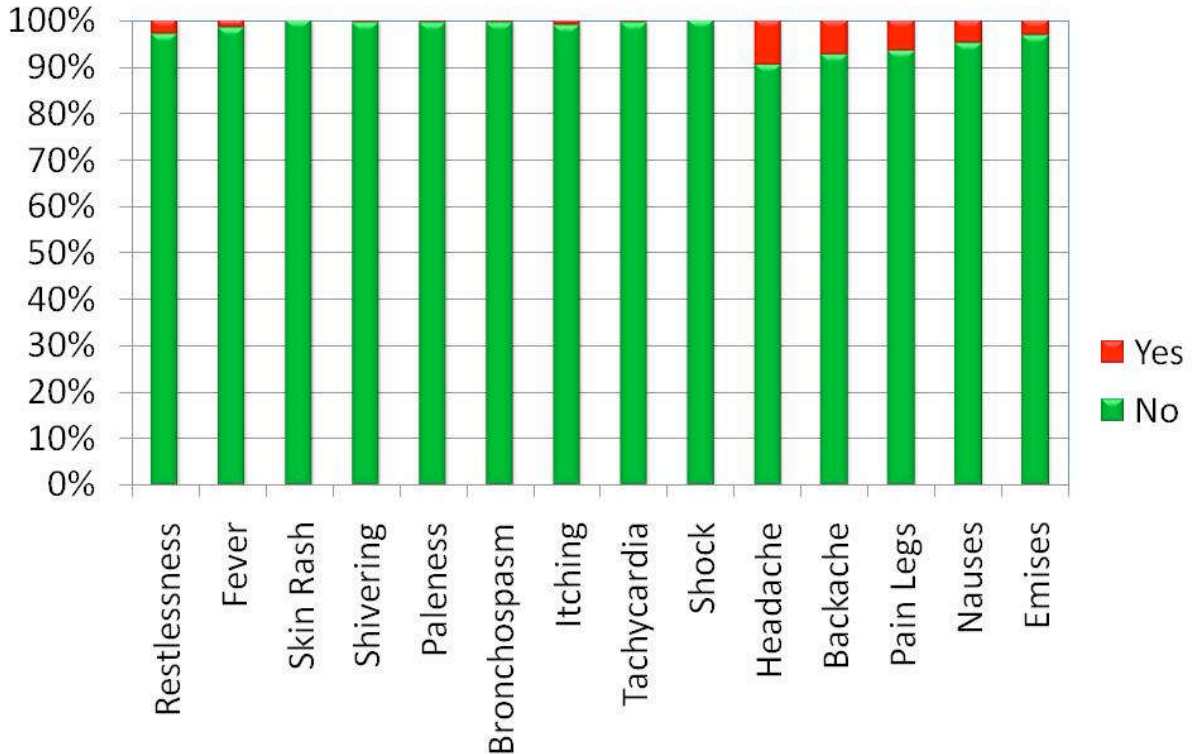
Study Population		Number Patients	All Headaches	Only PDPHA	Backaches	Author and group
1.	Children less than 10 years old	N=67	12 (18,0%)	3 (5,0%)	16 (24,0%)	University Pediatric Hospital Heidelberg Germany <sup>5</sup>
	Children 10 years old or more	N=45	18 (40,0%)	7 (16,0%)	29 (64,0%)	
2.	Adults for Diagnostics Mental illnesses	N=428		29 (6,78%)	13 (3,04%)	University of Washington USA <sup>16</sup>
3	Adults for diagnostics	N=106		16 (15,1%)		Department of Emerg. Medic. Indiana University School of Medicine USA <sup>21</sup>
4.	Adults for diagnostics	N=100		9 (9,0%)		University of Bonn Germany <sup>17</sup>
5.	Adults for diagn. traumatic	N=115		14 (12,2%)		Department of Neurology, University of Munich Germany <sup>22</sup>
	Adults for diagn a-traumatic	N=115		28 (24,4%)		
6.	Adults with MS for diagnostics	N=22		5 (22,7%)		University of Texas Southwestern Medical Center Dallas <sup>23</sup>
7.	Adults Spinal Anaesthesias	N=873		75 (7,35%)		Department of Anaesthesiology Odense University hosp. Denmark <sup>24</sup>
8.	Adults stem cell treatment	N=350	33 (9,4%)	13 (3,7%)	26 (7,4%)	XCell-center Cologne Germany

Out of 350 lumbar puncture procedures Xcell-center, only 9.4% reported headaches and 7.4% reported Back Pains. Table 2 presents the results of the Post Treatment Surveys in more detail concerning the frequency and severity of the reported headaches.

Headache category	No Headache	Happened once	Happened more than	Happened Daily	Total Number
No Headache complaints	317				317
Mild Headache complaints		9	2		11
Moderate Headache		7	3	1	11
Severe Headache		4	3	4	11
Percentage	317	20	8 (2,3%)	5	350

Diagram 1 presents the results of the Post Treatment Survey of XCell-center in more detail.

**Diagram 1: Overview Incidence Side Effects Survey Stem Cell treatment by Lumbar Puncture  
Xcell-center Cologne (n=350 patients)**



Besides headache and backache, there were no reports of skin rashes, tachycardia or bronchospasm. Mild fever was reported in 4 cases but didn't last longer than 1 day. The cause of the fever seems to be a short episode of an upper respiratory tract infection.

Of the 350 patients only 6 (1,7%) experienced some side effects lasting more than 10 days. The side effects lasting longer than 10 days were only reported by spinal cord injury patients. The reported complaints were mild backache and mild pain in the legs. 1 month after the treatment no patient reported any side effect.

## Discussion

Today, a few clinical trials have been accomplished using stem cells for transplantation. A small group of 6 patients with a complete spinal cord injury have been treated by autologous stem cells using the lumbar puncture procedure. This clinical trial has a follow-up of 3 years and until now no side effects or unexpected adverse reaction were observed<sup>6</sup>. Another study involved 9 complete spinal cord injury patients with a follow-up of 1 year. They observed major improvements and no side effects<sup>25</sup>. In both studies, MRI's didn't show any signs of malignancy<sup>6,25</sup>. Another observation comes from a phase I/II study with autologous stem cells and multiple sclerosis patients. 21 patients with multiple sclerosis were treated and followed for a period of 3 years. This study not only reported no unexpected side effects but showed also an improvement of the health situation of a part of the patients<sup>26</sup>. All these studies used lumbar puncture as procedure to inject the stem cells into the intrathecal space.

According to the Headache Classification Committee of the International Headache Society, headache after lumbar puncture is defined as bilateral headache that develop within 7 days after a lumbar Puncture and disappears within 14 days. The headache worsens within 15 minutes of resuming the upright position, disappears or improves within 30 minutes of resuming the recumbent position. In general Post Dural Puncture Headache lasts not more than 2 to 3 days. To give an estimation of the portion of Post Dural Puncture Headache within XCell-center, the categories "Headache happened more than once" and "Happened daily" are put together as an estimation. Within Xcell-center, the incidence of Post Dural Puncture Headache is estimated as low as 3,7% (13 cases out of 350 patients). Comparing with literature, this is a low incidence and shows again the safety of the procedure lumbar puncture. Besides headache and backache, 4 patients mentioned a short period of fever without skin rashes and without other complaints. The fever was mild and happened once. The cause of the fever was a short period of an upper respiratory tract infection.

Lumbar puncture as procedure to inject the stem cells in the intrathecal space is a safe and non-invasive treatment with promising results. The Post Treatment Survey has proven to be a good quality measurement to evaluate the patients and monitor the side effects.

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