

Autologous Stem Cell Transplantation by lumbar puncture:

A safety Follow-up in 870 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 870 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, 870 patients with a lumbar puncture as procedure for delivery of the stem cells were 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 11.9% (103 cases out of 870 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 useful tool to monitor the safety of the procedures.

Key Words

Autologous stem cells; lumbar puncture; therapy, safety;

Introduction

Lumbar puncture is a frequently performed procedure for diagnosis and therapy delivery¹. 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 removed². In general about one third of patients develop headaches after a lumbar puncture procedure³. Headache after lumbar puncture occurs more often in young adults⁴. On the other hand, complaints are reported less often after lumbar puncture procedure in young children⁵. 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 safe⁶⁻⁸ and the only side effects, mentioned are related by the procedure used to inject the stem cells into the target area⁹.

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^{10,11}. Complaints of rejection are fever, restlessness and skin rashes¹². 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).

Back pain varies between 22% and 45% and the occurrence of nausea varies between 14% and 20% ²⁰. In general the onset of the complaints begins 24 hours after the lumbar Puncture. The complaints are self limiting. The general duration of the complaints are seldom more than 2 to 5 days⁵. Table 1 shows a review of the incidence of Post Lumbar Puncture Headache.

| Table 1: Review of literature about Post Lumbare Puncture Headache and Backache | | | | | | |
|--|--|------------------------|----------------------|-------------------|------------------|--|
| Study Population | | Number Patients | All Headaches | Only PDPHA | Backaches | Author and group |
| 1. | Children less then 10 years old | N=67 | 12 (18,0%) | 3 (5,0%) | 16 (24,0%) | Univerity Pediatric Hospital Heidelberg Germany ⁵ |
| | 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 ¹⁶ |
| 3 | Adults for diagnostics | N=106 | | 16 (15.1%) | | Department of Emerg. Medic.Indiana University School of Medicine USA ²¹ |
| 4. | Adults for diagnostics | N=100 | | 9 (9.0%) | | University of Bonn Germany ¹⁷ |
| 5. | Adults for diagn. traumatic | N=115 | | 14 (12.2%) | | Department of Neurology, University of Munich Germany ²² |
| | 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 ²³ |
| 7. | Adults Spinal Anaesthesias | N=873 | | 75 (7.35%) | | Department of Anaesthesiology Odense University hosp.Denmark ²⁴ |
| 8. | Adults stem cell treatment | N=870 | 177 (21.3%) | 103 (11,9%) | 163 (18.7%) | XCell-Center Clinics Germany |

Out of 870 lumbar puncture procedures Xcell-center, 21.3% reported headaches and 18.7% 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 Once | Happened Daily | Total Number |
|--------------------------|-------------|---------------|-------------------------|----------------|--------------|
| No Headache complaints | 693 | | | | 693 |
| Mild Headache complaints | | 32 | 23 | 4 | 59 |
| Moderate Headache | | 12 | 47 | 14 | 73 |
| Severe Headache | | 3 | 21 | 21 | 48 |
| Percentage | 693 (79,7%) | 47 (5,4%) | 91 (10,5%) | 39 (4,4%) | 870 (100%) |

Diagram 1: Overview Incidence Side Effects Survey Stem Cell treatment by Lumbar Puncture XCell-Center Cologne and Dusseldorf (n=870 patients)

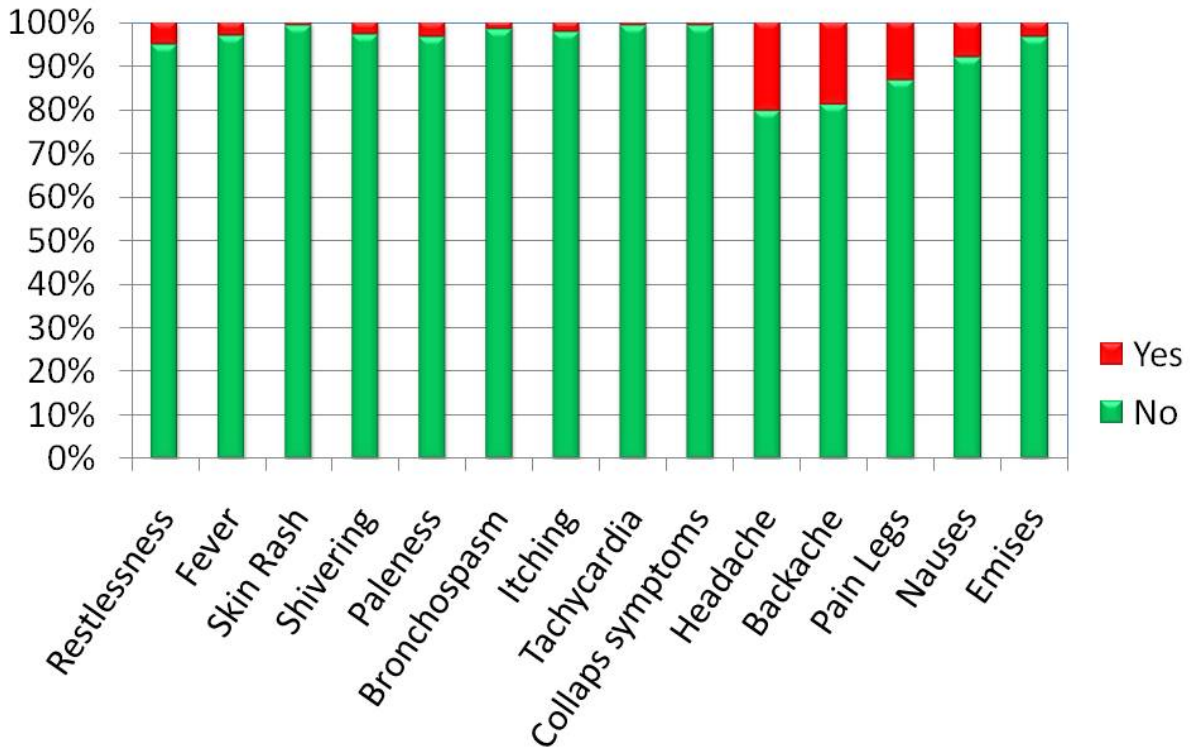


Diagram 1 presents the results of the Post Treatment Survey of XCell-Center in more detail.

Besides headache and backache, there were only 7 reports of mild skin rashes and 8 cases of temporary tachycardia. Mild fever was reported but didn't last longer than 3 days. The cause of fever seems to be short episodes of an upper respiratory tract infection.

From the 870 samples tested on microbiological contamination only two were positive.

Individual follow-up with the two patients with a positive sample test done by a physician of XCell-Center didn't show side effects at all (special attention to exclude Fever and Meningitis).

Of the 870 patients only 12 (2.1%) experienced some side effects lasting more than 10 days. The side effects lasting longer than 10 days were only reported by spinal cord injury and ALS 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 observed⁶. Another study involved 9 complete spinal cord injury patients with a follow-up of 1 year. They observed major improvements and no side effects²⁵. In both studies, MRI's didn't show any signs of malignancy^{6, 25}. 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 patients²⁶. 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” in the qualification moderate and severe and “Happened daily” in the qualification mild, moderate and severe are put together as an estimation. Within XCell-Center, the incidence of Post Dural Puncture Headache is estimated as low as 11.9% (103 cases out of 870 patients). Comparing with literature, this is a comparable to literature incidence and shows again the safety of the procedure lumbar puncture. Besides headache and backache, a small number of patients mentioned a short period of fever without skin rashes and without other complaints. The fever was mild and in the majority of the cases happened only 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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