

Safety Report Lumbar Puncture Procedure within XCell-Center Cologne

Introduction

Lumbar puncture is a frequently performed procedure for diagnosis and therapy delivery. 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. In general about one third of patients develop headaches after a lumbar puncture procedure (Evans RW 2000;55). Headache after lumbar puncture occurs more often in young adults (Leibold RA 1993;22). On the other hand, complaints are reported less often after lumbar puncture procedure in young children (Ebinger F 2004;113). Within Xcell-center , Lumbar Puncture is one of the most often used procedures to inject autologous stem cells into the spinal cavity. In literature, autologous stem cell delivery is safe and the only side effects, mentioned are related by the procedure used to inject the stem cells into the target area (Bakshi A 2004;3). 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.

Methods

Within Xcell-center, all the patients treated with stem cells are followed to detect unexpected side effects. The follow-up can be divided in a post treatment survey (first day of the stem cell delivery), a first 10 day side effect survey (This survey take place in the third week after stem cell delivery) and a 3 months survey (asking for long term side effects and first effects of the treatment). These procedures were established from the beginning of Xcell-center. The last 350 patients treated in 2008 with stem cells using Lumbar Puncture as delivery procedure were analyzed using the Side effect forms. Most studies only describe Post Dural Puncture Headache (classical headache describe using LP procedures). To give an estimation of the safety of the Lumbar Puncture Procedures within XCell-center Cologne, the results of the side effect monitoring of 350 patients of Xcell-center were compared with the results mentioned in the literature (table Literature review). Every patient undergoing autologous stem cell treatment is asked to fill in a side effect form covering the side effects within 10 days and the side effects lasting longer than 10 days. Xcell-center uses questions discriminating the headache complaints in three categories (mild, moderate and severe). The duration is divided in categories concerning the items once occurring, more than once occurring, or occurring every day.

Results

In summary, The incidence of Post Dural Puncture Headache, mentioned in literature, varies between 5,0% within children under the age of 10 until 24,4% within adults using a traumatic needle for diagnostics procedures. Back pain varies between 22% and 45% and the occurrence of Nausea varies between 14% and 20%. (Kruesi MJP 1988;25). 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 days (Ebinger F 2004;113).

Review literature

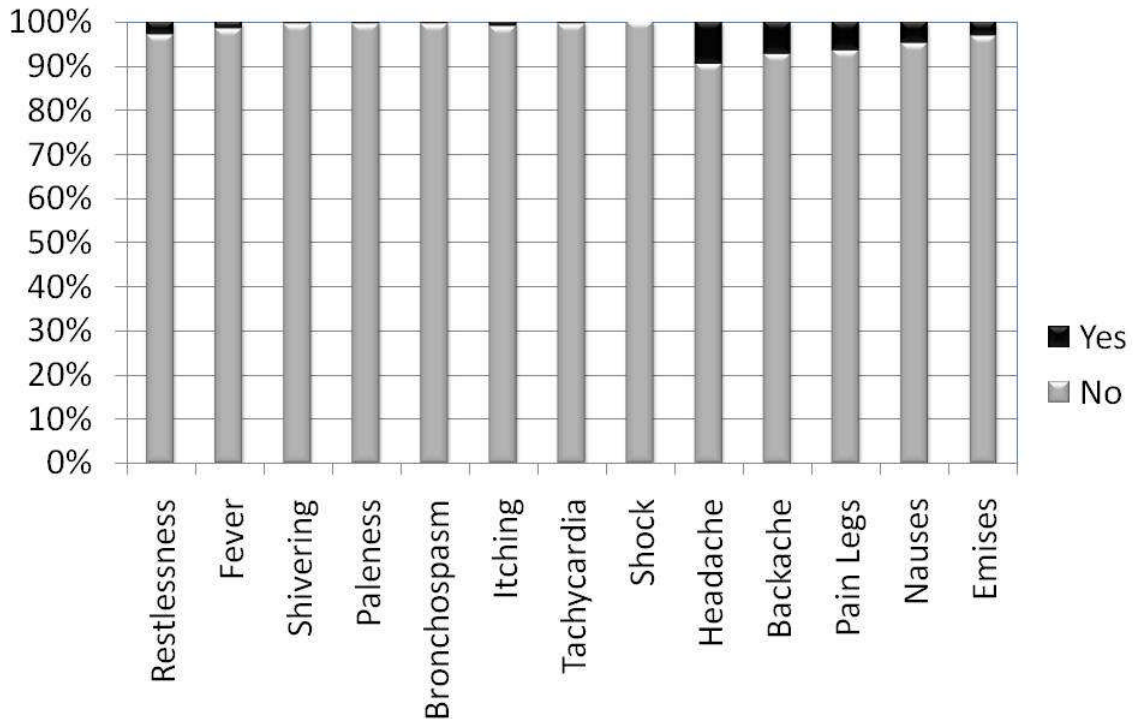
Study Population		Number Patients	All Headaches	Only PDPHA	Backaches	Author and group
1.	Children less than 10 years old	N=67	12 (18,0%)	3 (5,0%)	16 (24,0%)	Ebinger,F; Univerity Pediatric Hospital Heidelberg Germany (Ebinger F 2004;113)
	Children 10 years old or more	N=45	18 (40,0%)	7 (16,0%)	29 (64,0%)	
2.	Adults for Diagnostics Mental illnesses	N=428		29 (6,78%)	13 (3,04%)	Peskind, E; University of Washington USA (Peskind ER 2005;19)
3	Adults for diagnostics	N=106		16 (15,1%)		Seupaul RA; Department of Emergency Medicine Indiana University School of Medicine USA (Seupaul RA 2005;23)
4.	Adults for diagnostics	N=100		9 (9,0%)		Popp,J; University of Bonn Germany (Popp J 2007;78)
5.	Adults for diagnostics atraumatic needle	N=115		14 (12,2%)		Strupp M; Department of Neurology, University of Munich Germany (Strupp M 2001;57)
	Adults for diagnostics traumatic needle	N=115		28 (24,4%)		
6.	Adults with MS for diagnostics	N=22		5 (22,7%)		Stuve, O; University of Texas Southwestern Medical Center Dallas (Stuve O 2007;64)
7.	Adults Spinal Anaesthesias	N=873		75 (7,35%)		Lybecker, H; Department of Anaesthesiology Odense University hospital Denmark (Lybecker H 1990;70)
8.	Adults stem cell treatment	N=350	33 (9,4%)	13 (3,7%)	26 (7,4%)	Report safety XCell-center Cologne Germany (de Munter, J)

Out of 350 Lumbar Puncture procedures Xcell-center, only 9.4% reported Headache and 7.4% reported Back Pain. Table 1 presents the results of the Side effect Survey in more detail concerning Headache.

Headache category	No Headache	Happened Once	Happened more than Once	Happened Daily	Total number
No Headache complaints	317				317
Mild Headache complaints		9	2		11
Moderate Headache complaints		7	3	1	11
Severe Headache complaints		4	3	4	11
Percentage	317 (90,6%)	20 (5,7%)	8 (2,3%)	5 (1,4%)	350 (100%)

Diagram 1 presents the results of the Side Effect Survey of XCell-center in more detail. The survey covers all kind of side effects mentioned in relation to Lumbar Puncture procedures.

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



Of the 350 patients only 6 (1,7%) experienced some side effects lasting more than 10 days. Back pain and pain in the legs were mentioned as side effect lasting more than 10 days.

Conclusion

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 (Olson J 2004;24). 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).

References

Bakshi A, Hunter C, Swanger S, et al. "Minimally invasive delivery of stem cells for spinal cord injury: advantages of the lumbar puncture technique." *J Neurosurg*, 2004;3: 330-337.

Ebinger F, Kosel K, Pietz J, Rating D,. "Headache and Backache after Lumbar Puncture in children and Adolescents: a prospective Study ." *Pediatrics*, 2004;113: 1588-92.

Evans RW, Armon C, Frohman EM, et al. "Assessment: prevention of post-lumbar puncture Headache." *Neurology*, 2000;55: 909-914.

Kruesi MJP, Swedo SE, Coffey ML, Hamburger SD, Rapoport JL. "Objective and subjective side effects of research lumbar puncture in children and adolescents;" *Psychiatric Research*, 1988;25: 59-63.

Leibold RA, Yealy DM, Coppola M, et al. "Post-dural puncture headache: characteristics, management and prevention." *Ann Emerg Med*, 1993;22: 1863-70.

Lybecker H, Moller JT, May JT, Nielsen HK. "Incidence and prediction of post dural puncture headache: a prospective study of 1021 spinal anesthetics;" *Anesth Analg*, 1990;70: 389-394.

Olson J, Boussier M, Diener H, et al. "The International Classification of headache Disorders." *Cephalalgia*, 2004;24: 9-160.

Peskind ER, Riekse R, Quinn JF, Kaye J, et al. "safety and Acceptability of the Research Lumbar Puncture." *Alzheimer Dis Assoc Disord*, 2005;19: 220-225.

Popp J, Freymann MRK, Jessen F. "Ambulante durchfuhrung einer diagnostischen lumbalpunktion in der gedachtnissprechstunde." *Nervenarzt*, 2007;78: 547-551.

Seupaul RA, Somerville GG, Viscusi C, et al. "Prevalence of postdural puncture headache after ED performed lumbar puncture." *Am J Emerg*, 2005;23: 913-15.

Strupp M, Schueler O, Straube A, et al. "Atraumatic Sprotte needle reduces the incidence of post-lumbar puncture headaches." *Neurology*, 2001;57: 2310-2312.

Stuve O, Cravens PD, Mahendra PS, Frohman EM, et al. "High Incidence of post-lumbar puncture headaches in patients with MS treated with natalizumab: Role of intrathecal leukocytes." *Arch Neurology*, 2007;64: 1055-6.

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