

#500 -The Effect of Cerebrolysin on Neurogenic Detrusor Overactivity after Spinal Cord Injury A urodynamic study in female Wistar Rats

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INTRODUCTION

Neurogenic detrusor overactivity (NDO) is an important clinical problem. It refers to urinary bladder dysfunction that is mostly caused by spinal cord injury (SCI) or injuries to the central nervous system. Most of SCI patients show a functional bladder outlet obstruction caused by detrusor sphincter dyssynergia. This situation results in high intravesical pressures which can cause urine reflux to the kidneys and kidney function damage. Cerebrolysin is a drug that consists of a mixture of peptides with low molecular weight purified from pig brain. This drug has pharmacologic properties that are similar to endogenous neurotrophic factors. Cerebrolysin is thought to have a potential neuroprotective and neurotrophic properties and is the only drug currently accessible for clinical use which contains some of important neurotrophic factors. Cerebrolysin is used with the purpose of regeneration of neurons and induction of neuroprotection in neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, Alzheimer's disease, dementia, and acute or chronic stroke. In this study, we evaluated the effect of Cerebrolysin on bladder function after SCI, using urodynamic measurements in rats.

METHODS

Sixty female rats (weighing 220-250 g) were used in our study. All experimental rats (n=60) were randomly divided into 10 groups with n=6 in each group. We distinguished the following groups: 1. control, 2. sham-operated, 3. acute SCI+saline (1 week), 4. chronic SCI+saline (4 weeks), 5. acute SCI+Cerebrolysin 1ml/kg, 6. acute SCI+Cerebrolysin 2.5ml/kg, 7. acute SCI+Cerebrolysin 5ml/kg, 8. chronic SCI+Cerebrolysin 1ml/kg, 9. chronic SCI+Cerebrolysin 2.5ml/kg, 10. chronic SCI+Cerebrolysin 5ml/kg. In the acute SCI group, Cerebrolysin was injected i.p. every day until 7 days (1 week), after the induction of complete transection model at T9-T10 segment of rat spinal cord. So in this group, drug interventions were started immediately. In chronic spinal cord injury group, Cerebrolysin was injected i.p. every day until 28 days (4 week). To reveal the influence of Cerebrolysin after SCI on bladder function, bladder and spinal cord tissues, we evaluated urodynamic parameters, of the rats in the different groups. Awake urodynamic measurements were conducted in experimental groups after 1 and 4 weeks as follows: under 2% isoflurane anaesthesia, two transvesical catheters were inserted into the rat bladder in order to measure urodynamic parameters. Changes in intravesical pressure were recorded to evaluate and compare urodynamic parameters in experimental groups. The following parameters were used to evaluate all the rats over the 30–60-min time period: baseline bladder pressure; threshold volume; maximum voiding pressure and bladder capacity

Variable / Groups (acute)	Control	Sham	SCI+saline	SCI+Cerebr. 1 µg	SCI+Cerebr. 2.5 µg	SCI+Cerebr. 5 µg
Peak pressure (cm H₂O)	22	14	11	20	29	42
Baseline pressure (cm H ₂ O)	6.8277	4.4043	3.0875	14.505	13.09	18.75
Frequency of voiding (time/min)	0.2651	1.0761	3.3632	0.0521	0.0179	0.0751
Maximum void pressure (cm H ₂ O)	13	7	3	8	10	12
Bladder contraction (time/min)	0.1767	0.3154	0.0896	0.7304	2.817	5.1077
Amplitude of contraction (cm H ₂ O)	13.4	11.471	10.5	18.571	14.127	19.612
Inter-contraction interval (sec)	324.5	188.71	429	82.071	21.287	11.662
Bladder compliance (ml/ cm H ₂ O)	0.1414	0.0755	0.1605	0.0333	0.0173	0.0041

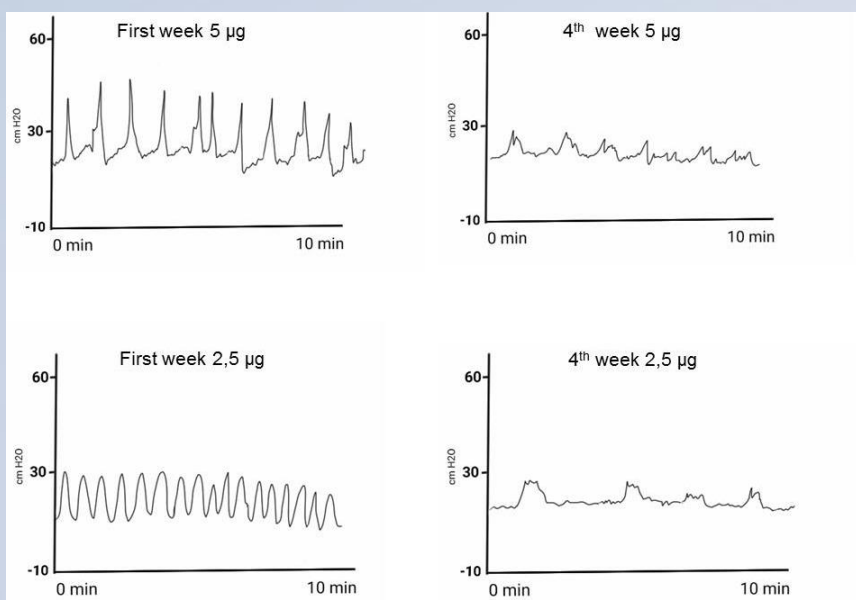
RESULTS

The pattern of bladder reflex activity in spinal intact and SCI rats with different doses of Cerebrolysin for one week and 4 weeks were evaluated and compared. We investigated the following parameters: frequency, peak pressure, baseline pressure and amplitude of bladder contractions in both groups.

Cerebrolysin injection in a dose of 1µg didn't make any changes in urodynamic parameters in both groups. However, infusion of 5 µg Cerebrolysin made NDO changes with high pressures and amplitudes.

In the group with 2,5 µg infusion of Cerebrolysin, bladder contractions with low amplitude but moderate pressure were found (figure1). At the end of fourth week, NDO appeared in the no-intervention and the 1µg-group. In addition, the acute phase NDO relatively improved in the 2,5 µg group.

Our results show, that Cerebrolysin as a mixed growth factor, might be able to inhibit the emergence of NDO in SCI female rats. Cerebrolysin injection in a dose of 1µg had no urodynamic effects in our study. However, infusion of 5 µg Cerebrolysin induces high pressures and amplitudes. Surprisingly, the bladder pressure pattern the in 5 µg infused rats showed a comparable pattern with the group of spinal cord intact rats. However, the 5 µg dose appears to be too high for the study animals and unfortunately half of these animals did not survive at the end of the study period.



CONCLUSIONS

Our preliminary results show that Cerebrolysin as a mixed growth factor, might be able to inhibit the emergence of NDO. These findings can open new doors in the management of NDO in SCI patients.