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THE EFFECT OF MEMANTINE ON DETRUSOR OVERACTIVITY IN RATS WITH SPINAL CORD INJURY

Hypothesis / aims of study

Spinal cord injury results not only from the initial direct injury, but also from secondary damage via excitatory amino acid cascade (i.e. glutamate). High levels of exctracellular glutamate bind to N-methyl-D-aspartate (NMDA) and AMPA-Kainate receptors causing an increase in intracellular calcium that activates proteases, endonucleases and generates free radicals, all leading to neuronal cell death (1). Memantine acts as an open channel blocker, that enters the channel pore and sterically occludes the ion pathway (2). We evaluated the effect of memantine (glutamate receptor antagonist) on overactive detrusor after spinal cord injury in rats.

Study design, materials and methods

Ethical approval for the study was granted by the University Ethics Committee. Included in this study were 26 adult female wistar rats. Twelve animals served as normal controls, while 14 underwent spinal cord transection (clip compression technique) at the 10th thoracic vertebra. Fifteen days after spinal cord injury (SCI) 14 rats underwent filling cystometrogram (CMG) to confirm overactive detrusor, while another 12 served as normal control. Filling cystometrogram was performed in SCI animals before and after memantine treatment (16mg/kg, intraperitonealy). Parameters measured included voiding volume (VV), micturition pressure (MP), resting bladder pressure (RBP), a period between micturation (PM), and maximum pressure of overactive detrusor during filling period ($OADP_{mx}$). The Mann-Whitney U test or Wilcoxon signed-rank test was used when appropriate for statistical data analysis. For all statistical tests, $P<0.05$ was considered significant.

Results

The mortality rate was 66 % in SCI rats. Normal rats showed stable CMG; RP was 6.66± 3.02cmH2O, MP of 24.91±10.82cmH2O, PM of 38.33±8.30sc, and VV of 100-300µl. Compared with normal rats, SCI rats had high MP (44.37±21.89 versus 24.91±10.82cmH2O, $P<0.05$) and RP (14.75± 8.24 versus 6.66±3.02cmH2O, $P<0.05$). PM was slightly higher (48.25±41.32 versus 38.33±8.30sc, $P>0.05$) in SCI rats than normal animals. Overactive detrusor was found in 57.1% of the rats following SCI after fifteen days. Overactive detrusor resolved in 62.5 % of the animals that received 16mg/kg. memantine, intraperitonealy. All parameters for SCI rats were summarised in table 1

Table1. Parameters before memantine and after therapy in SCI rats.

Parameters	Before memantine (mean±SD)	(Range)	After memantine (Mean±SD)	(Range)	P value
MP(cmH2O)	44.37 ± 21.89	(20-91)	30.87 ± 14.74	(19-63)	<0.05
PM(sc)	48.25 ± 41.32	(15-140)	65.37 ± 31.25	(30-120)	>0.05
RP(cmH2O)	14.75 ± 8.24	(6-29)	10.12 ± 7.37	(5-22)	<0.05
$OADP_{mx}$ cmH2O	*	(20-92)	*	(0-38)	*

*No SD was given related to a smaller extent for results of $OADP_{mx}$

Interpretation of results

Overactive detrusor was found in 57.1% of the rats following SCI after fifteen days. More time may be necessary to see a greater amount of overactive detrusor following SCI in rats. On the other hand, the high mortality rate has restricted the time for the developing of overactive detrusor in SCI rats. Memantine as an open channel blocker eliminated overactive detrusor in 62.5 % of the rats after SCI. It is likely that this effect was due to the reduction of intracellular calcium by memantine (glutamate receptor antagonist).

Concluding message

Memantine may be an attractive way of treating overactive bladder. If this theory is supported by further clinical studies, memantine may be an alternative therapy besides antimuscarinic treatments for detrusor overactivity.

References

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