**Title of the project:** The influence of experimental gastrointestinal injury and inflammation on pharmacokinetics of Alzheimer disease drugs

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**Principal Investigator:** Jan Bureš

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### Summary of 2019 results

**Title of the presentation:** The Pharmacokinetic Parameters and the Effect of a Single and Repeated Doses of Memantine on Gastric Myoelectric Activity in Experimental Pigs

**Authors:** J Bures, J Kvetina, V Radocha, I Tacheci, E Peterova, D Herman, R Dolezal, M Kopacova, S Rejchrt, T Douda, V Sestak, L Douda, J Zdarova Karasova

Memantine is an antagonist of the N-methyl-D-aspartate type of glutamate receptors. Memantine administration is associated with different gastrointestinal dysmotility side effects (vomiting, diarrhoea, constipation, motor-mediated abdominal pain), thus limiting its clinical use. Mechanism of these motility disorders has not been clarified yet.

The aim of this study was to evaluate the impact of a single and repeated doses of memantine on porcine gastric myoelectric activity evaluated by means of electrogastrography (EGG).

Single dose of memantine significantly increased DF, from basic values (1.65±1.05 cycles per min.) to 2.86 cpm after 30 min. (p=0.008), lasting till 75 min. (p=0.014). Basal power (median 452; inter-quartile range 280 – 1312 μV^2) raised after 15 min. (median 827; IQR 224 – 2769; p=0.386; NS), lasting next 30 min. Repetitively administrated memantine caused important gastric arrhythmia. Basal DF after single and repeated administration was not different, however, a DF increase in the second part was more prominent (up to 3.18±2.16 after 15 and 30 min., p<0.001). In comparison with a single dose, basal power was significantly higher after repetitively administrated memantine (median 3940; IQR 695 – 15023 μV^2; p<0.001). Next dose of 20 mg memantine in the second part induced a prominent drop of power after 15 min. (median 541; IQR 328 – 2280 μV^2; p<0.001), lasting till 120 min. (p<0.001).

Both single and repeated doses of memantine increased DF. Severe gastric arrhythmia and long-lasting low power after repeated administration might explain possible gastric dysmotility side effects in the chronic use of memantine.

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