THE ORALLY EFFECTIVE MIXTURE OF SOD AND GLIADIN

GlisODin® PROTECTS AGAINST OXIDATIVE DNA DAMAGE

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Background:
Generation of oxygen-derived radicals has been demonstrated to be the major mechanism of ischemia-reperfusion induced damage [1]. Reactive oxygen species interact with DNA leading to structural alteration [2]. Recently, we showed that GlisODin®, an orally effective mixture of SOD and wheat gliadin, protected against hyperbaric oxygen (HBO)-induced DNA damage assessed by single cell gel electrophoresis (comet assay) [4]. Since DNA damage was less marked than in previous studies [3], we investigated whether GlisODin® is also protective when during more severe oxidative stress.

Materials and Methods:
After 2 weeks of feeding once a day with 1250 IU of GlisODin® (n = 9) or vehicle (n = 5) blood samples were taken from swine body weight 50 (47-53) kg. DNA damage (tail moment in the alkaline version of the comet assay was evaluated in isolated lymphocytes (Ficoll gradient) before and after HBO exposure (2 hrs at 4 bar O2) (GlisODin®n=9, Vehicle n=5). Comet assay was performed as well in whole blood samples taken at different time points (before and after 30 minutes thoracic aortic cross-clamping as well as 2 and 4 hours after declamping) during thoracic aortic surgery (GlisODin®n=8, Vehicle n=7). Plasma 8-isoprostane (8-epi Prostaglandin F2α) concentrations as a direct marker of lipid peroxidation were determined using an enzyme immunoassay kit (Camygen Chemicals, Ann Arbor, MI) in portal (PV) and hepatic veins (HV) blood before and after aortic cross clamping. Antioxidant enzyme SOD (RANSOD kit, Randox Laboratories Ltd, U.K.) and catalase activity (assayed by a method in which the disappearance of peroxide is followed spectrophotometrically) were assessed on whole blood samples taken during aortic cross clamping and on lymphocytes isolated before and after HBO exposure. Data are median (range). After exclusion of normal distribution data using a Kolmogorov-Smirnov-test, time dependent differences within groups during aortic surgery were analyzed with a Friedman repeated measures ANOVA and, if appropriate, by a Dunn’s test. Differences before and after HBO exposure were analyzed with a Wilcoxon signed rank test. Inter-group differences were analyzed with Mann-Whitney rank sum test.

Results:
There was no difference in DNA damage before exposure to HBO (p = 0.255 GlisODin® vs. Vehicle). GlisODin®bound (tail moment from 0.08 (0.06-0.12) to 0.11 (0.07-0.23), p = 0.020) the otherwise marked increase (Vehicle: tail moment from 0.11 (0.09-0.13) to 0.43 (0.40-0.73), p = 0.063) in DNA strand breaks after HBO exposure (p = 0.005 GlisODin® vs. Vehicle after HBO). GlisODin® also reduced oxidative DNA damage related to surgical stress and ischemia-reperfusion after aortic clamping (tail moment from 0.09 (0.08-0.11) to 0.12 (0.11-0.14), p = 0.023) in comparison to Vehicle (tail moment from 0.12 (0.11-0.15) to 0.48 (0.35-0.60), p = 0.031) resulting in a statistically significant intergroup difference 2 hrs after declamping (p = 0.021, GlisODin® vs. Vehicle). While there was no intergroup difference in the baseline values of isoprostane levels (p = 0.391), there was a significant increase in isoprostane levels among groups after HBO exposure (p = 0.033) and portal venous samples (0.006). No such effect was observed in GlisODin® group. Neither SOD nor catalase activities were significantly affected by HBO exposure (p > 0.05, GlisODin® vs. Vehicle after HBO).

Conclusions:
 Pretreatment with the new nutritional formula of SOD-wheat gliadin (GlisODin®) allows to prevent oxidative DNA damage related to HBO treatment or ischemia-reperfusion injury. The unaltered SOD activities after oral SOD ingestion are probably due to relatively low SOD supplementation when compared to total blood SOD pool [3,5]. The effect of SOD, thus, most likely results from an immune response and through a nitric oxide dependent mechanism [5].

References:


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B. Hauser was supported by the Alexander von Humboldt Foundation

* before clamping: 2 hrs after declamping