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Effect of indometacin pretreatment on protamine sulfate-mediated relaxation of the isolated rat uterus: the role of the antioxidative defense system

Jelena Kordić-Bojinović[1], Zorana Oreščanin-Dušić[2], Marija Slavić[2], Ratko Radojičić[3], Mihajlo Spasić[2], Slobodan R. Milovanović[4], Duško Blagojević[2]

[1]High Medical School "Milutin Milanković", Belgrade, Serbia

[2]Department of Physiology, Institute for Biological Research, "Siniša Stanković", University of Belgrade, Blvd. Despota Stefana 142, 11000 Belgrade, Serbia

[3]Biological Faculty, University of Belgrade, Belgrade, Serbia

[4]Department of Pharmacology, Faculty of Medicine, University of East Sarajevo, Studentska bb, 73300 Foca, Republic of Srpska, Bosnia and Herzegovina

Correspondence: Zorana Oreščanin-Dušić, e- mail: zoranaor@ibiss.bg.ac.rs

Abstract:
Previous results in this laboratory indicate that protamine sulfate (PS) evokes dose-dependent relaxation of both spontaneous and calcium ion-induced uterus activity mediated predominantly by potassium channels and, to a small extent, *via* β-adrenergic receptors or nitric oxide (NO)-dependent pathways. Indometacin is a nonselective inhibitor of cyclooxygenase (COX 1 and COX 2) that has the ability to delay premature labor by reducing uterine contractions through the inhibition of prostanglandin synthesis in the uterus. This study investigates the effects of indometacin (0.1 and 1 μg/ml) pretreatment on the PS-induced relaxation of isolated uterine smooth muscle.
Indometacin pretreatment *per se* did not change the activity of the uteri. However, indometacin significantly increased PS-induced relaxation of spontaneous uterine contractions. Indometacin pretreatment significantly decreased the magnitude and slope of PS-induced relaxation of calcium ion-induced uterine contractions. Indometacin pretreatment increased CuZnSOD activity and slightly increased GR activity during spontaneous uterine contractions when compared to PS alone. In calcium ion-induced contractions, indometacin pretreatment increased CuZnSOD, GSH-Px and GR activities. These results suggest that, in addition to its COX inhibitory effects, indometacin influences the effects of PS. Therefore, it is possible that indometacin regulates diverse cell functions *via* its association with lipid membranes by altering micro-environments within the membranes. The above-mentioned processes appear to be partly mediated by redox processes involving ROS, lipid peroxides and antioxidant enzymes. The extent of the PS-mediated effect was different in spontaneous *versus* calcium ion-induced active uteri.

Key words:
indometacin, protmine sulfate, CuZnSOD, GSH-Px, GR, uterus