Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol10Issue3abst197P.pdf

P083

A new DHA derivative prevents heart-failure-induced atrial fibrillation in two experimental models.

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Atrial fibrillation (AF) is a common complication of heart failure and hypertension. By reduction of structural remodelling, upstream therapy is known to prevent the promotion and propagation of AF. The aim of the present study was to investigate the effects of a new pure docosahexaenoic acid derivative, i.e the nicotinyl ester of DHA, in two different experimental models of heart failure induced atria dysfunction. Firstly, nicotinyl ester of DHA administered at 5 g/day for 4 weeks significantly reduced the mean duration of AF induced by burst pacing in a dog model of tachypacing induced congestive heart failure. The duration of AF was significantly reduced from 989 ± 111 s in the vehicle group to 79 ± 59 s in the presence of nicotinyl ester of DHA treatment at 5 g/day. This dose of nicotinyl ester of DHA also significantly reduced the incidence of sustained AF (5 of 5 dogs in the vehicle group versus 1 of 5 in the nicotinyl ester of DHA 5 g/day group; $P<0.05$). Secondly, the atrial remodelling was investigated in a rat model of heart failure induced by 30 min occlusion of left descending coronary artery and 2 months reperfusion. The % of shortening fraction in the nicotinyl ester of DHA group (100 mg/kg p.o. daily) was significantly restored after 2 months (32.6 ± 7.4%, n=9 vs 17.6 ± 3.4%, n=9 in the vehicle group $P<0.01$ compared to 40.1 ± 3.1 %, n=8 in the sham group). Despite a marked tendency, the dilation of the left atria was only partially reduced (4.7 ± 0.2 mm in nicotinyl ester of DHA group vs 5.3 ± 0.2 mm in the vehicle group compared to 4.2 ± 0.1 mm in the sham group). Phosphorylation of connexin-43 (Cx43) was visualised by immunofluorescence in rat atria at the end of the study and quantified using the image J software. Nicotinyl ester of DHA reduced the de-phosphorylation of Cx43 (10.8 ± 1.6 u.a in nicotinyl ester of DHA group vs 8.2 ± 1.0 u.a in the vehicle group compared to 11.8 ± 1.3 u.a in the sham group). Finally, the present results show that treatment with nicotinyl ester of DHA reduced the atria and ventricular dilations, resynchronized the gap junction activity and reduced the AF duration in experimental models of heart failure. Thus, nicotinyl ester of DHA constitutes a promising new drug as up-stream therapy for the treatment of AF in patients with heart failure.