Scripta Scientifica Medica, vol.28, Suppl.1,pp.179-180

EFFECT OF THE CALCIUM CHANNEL BLOCKERS CINNARIZINE AND FLUNARIZINE ON GUT PASSAGE IN RATS

A. Belcheva, K. Marazova, V. Lozeva
Department of Pharmacology, Dobrich

In this decade calcium channel blockers have been employed successfully in the treatment of several cardiovascular disorders. Proceeding from the assumption that calcium is essential for smooth muscle contraction it is expected that calcium channel biockers could alter the motility of gastrointestinal tract. The aim of the present work was to determine and compare the effect of the diphenylpiperazine calcium channel blockers cinnarizine and flunarizine on spontaneous and altered by morphine (M), atropine (A) and carbachol (Cch) gut passage in rats. All experimental animals - 260 Wistar rats of either sex weighing 200-240 g were divided into 40 experimental and 1 control groups. Small intestine passage was determined by the Grisk method (1969). Suspension of carbo animalis (2 ml/100g) was applied per sondam and the rats were sacrificed 10 min later. Passage was given as the proportion of the gut containing the marker substance to the total length of the gut (from pylor to coecum). All animals had been deprived of food with free access to water for 24 h prior to decapitation. Cinnarizine (20 mg/kg i.p) and flunarizine (10 mg/kg i.p.) dissolved in the presence of twin 80 were introduced alone as well as 1 h before and 1 h after the alterating agents: M (10 and 20 mg/kg i.p.), A (0.1 and 0.5 mg/kg i.p.) and Cch (10 and 50 μg/kg i.p.). Statistical evaluation was performed by means of the Student's test for paired data. The effects of the pretreatment with cinnarizine and flunarizine are presented on table 1.

M causes a dose-dependent significant decrease in gut motility on the 1st h. Pretreatment with cinnarizine or flunarizine does not alter the effect of the drug. A reduces gut passage significantly in both used doses on the 1st h. Pretreatment with cinnarizine overcomes the reduction. Gut passage is accelerated significantly by 35,5% towards A 0,1 mg/kg and by 24,4% towards A 0,5 mg/kg. No effect of flunarizine is obtained in this case. We do not find significant changes in gut motility on the 1st h after Cch application. Pretreatment with cinnarizine enhances small intestine motility so that gut passage increases significantly compared to controls.

The effects of cinnarizine and flunarizine on gut passage when

applied 1 h after the alterating agents are presented on table 2. The decreased by M motility remains low on the 2nd hour. The application of cinnarizine or flunarizine does not change significantly this effect. Passage reduction caused by A persists on the 2nd h. Cinnarizine increases gut motility significantly by 27,4% towards A 0,1 mg/kg and by 17,7% towards A 0,5 mg/kg, so that passage reaches control value. Flunarizine increases passage significantly by 35,5% towards A 0,5 mg/kg. The effect of Cch on gut passage on the 2nd h is negligible. Cinnarizine and flunarizine enhance gut passage by 10,7% and 15,2%, resp., so that passage becomes significantly higher towards controls. Cinarizine alone accelerates gut passage significantly by 18,6% on the 1st h after its application only. Flunarizine does not affect gut passage significantly (tables 1 and 2).

Table 1. Effect of cinnarizine and flunarizine pretreatment on gut passsage altered by M, A and Cch (in %)

sub-stances	vehiculum 0.2 ml/kg	morphine 1 hour 10 mg/kg	morphine 1 hour 20 mg/kg	atropine 1hour 0,1 mg/kg	atropine 1hour 0,5 mg/kg	carbachol 1hour 10 µg/kg	carbachol 1hour 50 µg/kg
	50,82 ± 1,3 (n = 37)	27,76[a] ±1,3 (n = 10)	17,23[a] ±0,8 (n = 12)	35,43[a] ±2,0 (n = 14)	31,38[a] ±1,7 (n = 17)	50,81 ±2,0 (n = 10)	49,69 ±2,0 (n = 18)
cinnarizine 20 mg/kg 2h	50,19 ±2,0 (n = 26)	24,07[a] ± 2,7 (n = 6)	17,98[a] ± 0,4 (n = 6)	47,99[d] ± 2,7 (n = 8)	39,05[a e] ± 0,7 (n = 9)	63,05[b e] ± 5,3 (n = 5)	64,80[a e] ± 3,4 (n = 5)
flunarizine 10mg/kg 2h	51,68 ± 3,0 (n = 10)	34,55[a] ± 5,0 (n = 6)	18,90[a] ± 3,4 (n = 6)	36,56[a] ± 2,5 (n = 6)	35,81[a] ± 1,3 (n = 5)	48,47 ± 4,0 (n = 5)	52,45 ± 5,5 (n = 6)

Table 2. Effect of cinnarizine and flunarizine on gut passage when applied 1 hour after M, A and Cch (in %)

sub-stances	vehiculum 0.2 ml/kg	morphine 2 hours 10 mg/kg	morphine 2 hours 20 mg/kg	atropine 2 hours 0,1 mg/kg	atropine 2 hours 0,5 mg/kg	carbachol 2 hours 10 µg/kg	carbachol 2 hours 50 µg/kg
	50,82 ± 1,3 (n = 37)	39,85[a] ±2,6 (n = 13)	25,57[a] ±3,3 (n = 12)	43,82[b] ±2,2 (n = 14)	37,20[a] ±2,3 (n = 13)	56,27 ±4,5 (n = 10)	48,60 ±3,5 (n = 12)
cinnarizine 20 mg/kg 1h	60,28[a] ±2,5 (n = 20)	34,54[a] ± 5,6 (n = 6)	28,54[a] ± 4,6 (n = 6)	55,84[e] ± 2,7 (n = 10)	43,80[c] ± 2,7 (n = 10)	62,28[c] ± 9,4 (n = 6)	58,30 ± 4,5 (n = 6)
flunarizine 10mg/kg 1h	46,98 ±2,5 (n = 11)	40,57[b] ± 1,8 (n = 6)	31,36[a] ± 3,0 (n = 8)	51,10 ± 5,8 (n = 7)	50,42[e] ± 3,1 (n = 6)	64,83[a] ± 1,5 (n = 5)	51,52 ± 3,2 (n = 6)

$a_p < 0{,}001$ vs control $b_p < 0{,}01$ vs control $c_p < 0{,}05$ vs control
$d_p < 0{,}001$ vs test-substance $e_p < 0{,}01$