CHANGES IN PROSTAGLADIN E LEVELS IN ARTERIAL BLOOD AND CEREBROSPINAL FLUID DURING HYPO- AND HYPERCAPNIA

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A considerable increase was found in the concentration of prostaglandins of type E (PGE) in the CSF and arterial blood of cats during hypocapnia for 3 min. During hypocapnia for 30 min the original PGE level was restored. During hypercapnia for 3 min the PGE concentration was increased in the CSF compared with the control, but reduced in the arterial blood. After hypercapnia for 30 min the PGE concentration in the CSF and blood was reduced below its level after 3 min, and later it fell below the basal level. It is suggested that during hypocapnia PGE limit its constrictor effect on the cerebral vessels, whereas during hypercapnia they facilitate the response of the vessels to CO_2.

KEY WORDS: prostaglandins; cerebral vessels; hypocapnia; hypercapnia.

Inhibition of prostaglandin synthesis by indomethacin has been shown to cause changes in the responses of the cerebral vessels to hypo- and hypercapnia [1, 8, 12].

The object of this investigation was to study quantitative changes in the concentration of prostaglandins of type E (PGE) in arterial blood and CSF during hypo- and hypercapnia.

EXPERIMENTAL METHOD

Prostaglandins were extracted by the method of Unger et al [11] from arterial blood and CSF of 48 cats anesthetized with pentobarbital (25 mg/kg, intraperitoneally), artificially ventilated with nitrous oxide and oxygen, and immobilized with listhenon (5 mg/kg, intravenously, every 30 min). The state of the acid-base balance (ABB) of the arterial blood and CSF was monitored by a radiometer system. PGE were isolated by thin-layer chromatography [5], followed by biological tests [3] on strips of the stomach of 12 rats.

Hypocapnia was induced by hyperventilation and hypercapnia by the addition of 5% CO_2 to the inspired air. Control samples of arterial blood and CSF were taken during normocapnia and the remaining samples after exposure to hypocapnia and hypercapnia for 3 and 30 min.

The significance of differences between the results of the control and experimental groups were assessed by the Fisher–Student test.

EXPERIMENTAL RESULTS

During hypocapnia (Table 1) induced by hyperventilation the PGE concentration was significantly increased both in the CSF (by 2.8 times) and in the arterial blood (by 4.2 times). A parallel decrease was observed in the H^+ concentration in the CSF and arterial blood. After hypocapnia for 30 min the PGE concentration in the CSF was reduced almost to its original level, whereas in arterial blood, although considerably reduced, it still remained higher than in the control. As Table 1 shows, the H^+ concentration and pCO_2 of the arterial blood after hyperventilation for 30 min continued to fall, whereas the pH of the CSF had returned to its original level.

During hypercapnia (Table 2) as a result of inhalation of CO_2 for 3 min a considerable increase (by 5.8 times) was observed in the PGE concentration in the CSF, whereas in the blood it was almost unchanged. The values of ABB in the blood and CSF showed changes which corresponded to the conditions of hypercapnia.

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TABLE 1. Changes in PGE Concentration in Arterial Blood and CSF of Cats during Hypocapnia (M ± m, n = 20)

Experimental conditions	CSF		Arterial blood			
	pH	PGE, ng/ml	pH	PGE, ng/ml	pCO_2, mm Hg	pO_2, mm Hg
Control	7,40±0,01	0,5±0,18	7,40±0,01	1,36±0,24	28,00±0,89	155,00±12,72
Hyperventilation:						
3 min	7,50±0,01*	1,4±0,18*	7,53±0,01*	4,20±0.73*	14,42±0,94*	158,00±13,97
30 min	7,39±0,02	0,6±0,10	7,60±0,02*	2,70±0,50	13,42±0,68*	127,28±6,06

TABLE 2. Changes in PGE Concentration in Arterial Blood and CSF of Cats during Hypercapnia (M ± m; n = 13)

Experimental conditions	CSF		Arterial blood			
	pH	PGE, ng/ml	pH	PGE, ng/ml	pCO_2, mm Hg	pO_2, mm Hg
Control	7,40±0,01	0,50±0,18	7,39±0.02	1,36±0.24	30,57±0,35	141,16±9,06
Inhalation of CO_2:						
3 min	7,29±0,02*	2,90±0,60†	7,11±0.03†	1,30±0,41	68,10±5,30†	131,16±15,85
30 min	7,07±0,02 †	1,60±0,35*	6,97±0.03†	0.90±0.09	109,0±5.40*	141,66±13.17

*P < 0.05.

†P < 0.001.

After hypercapnia for 30 min, when pCO_2 and the H^+ concentration of the blood and CSF had increased further, the PGE concentration was reduced both in the blood and in the CSF compared with after exposure to hypercapnia for 3 min. A tendency for the PGE concentration in the arterial blood to fall below the control level was noted, i.e., basal PGE production was depressed, whereas the PGE concentration in the CSF continued to remain noticeably higher than it was initially.

The results show that hypocapnia, inducing cerebral vasoconstriction and reducing the blood flow, at the same time stimulates the production of PGE which, with their high vasodilator activity, counteract the vasoconstrictor effect of hypocapania. This may perhaps be one reason why the limit of the decrease in the cerebral blood flow in response to intensification of hypocapnia does not exceed 40% [13].

Measurements of pH on the brain surface showed that restoration of pH of the CSF during continuing hyperventilation takes place after 30 min [10]. Our own observations showed that at the 30th minute of hyperventilation, when pH of the CSF had fallen to the control level, the PGE concentration in the CSF was reduced. In the arterial blood, on the other hand, against the background of a stable pCO_2 and an increase in pH the PGE concentration fell, although it still remained above the control level. The mechanism of these mutual relationships is at present difficult to explain.

By contrast with hypocapnia, changes in the PGE concentration in the CSF and arterial blood during hypercapnia were opposite in character. The increase observed in the PGE concentration in the CSF could be the result of the direct effect of CO_2 (H^+), activating prostaglandin biosynthesis in the brain tissue or it could arise indirectly through catecholamines. Hypercapnia is known to have an excitatory effect on the sympathetic system. Starting from pCO_2 = 60 mm Hg the catecholamine titer in the arterial blood has been shown to rise progressively. Initially the concentrations of adrenalin and noradrenalin increase parallel to each other, but when pCO_2 reaches 100 mm Hg the noradrenalin level remains constant whereas adrenalin continues to rise [7]. Meanwhile, it has been shown that catecholamines can stimulate PGE biosynthesis and its liberation from cell structures [6]. However, the present experiments showed that notwithstanding the progressive increase in pCO_2 in the H^+ concentration in the CSF, the PGE concentration, which was increased in the CSF after 3 min of hypercapnia, later fell. A decrease in the prostaglandin level in the arterial blood below the basal value was observed. Consequently, the increase in the PGE concentration in the CSF was the result of the direct effect of CO_2 rather than an indirect effect through catecholamines. It is also known that CO_2 dilates the cerebral vessels [4]. In the light of the information obtained it can tentatively be suggested that prostaglandins play an important role in the maintenance of sensitivity of the receptors of the cerebral vessels to CO_2 (H^+), for in response to inhalation of CO_2 their concentration in the CSF rises, but when their biosynthesis is inhibited the response of the cerebral vessels to hypercapnia is lost [2, 8]. It has also been shown that maximal sensitivity of the brain vessels to CO_2 lies within pCO_2 values of 20 and 60 mm Hg [9]. In the present experiments, within these limits the PGE concentration in the CSF increased, whereas with an

increase in pCO_2 to 100 mm Hg it fell. This fact confirms the view that prostaglandins do not play the final role in maintenance of the sensitivity of the brain vessels to CO_2.

Analysis of the data showed that the PGE concentration in the CSF rises both in respiratory acidosis and in alkalosis. Meanwhile, during hypocapnia the cerebral blood flow is reduced, whereas during hypercapnia it is increased. Consequently, the role of PGE cannot be the same in these diametrically opposite states. It can tentatively be suggested that whereas in hypocapnia the role of PGE is to limit its constrictor effect on the brain vessels, in hypercapnia they prepare for and facilitate the response of the receptors of the brain vessels to CO_2.

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