STUDY ON THE CONCENTRATION OF CATECHOLAMINE CHANGE IN ISCHEMIC RAT CORTEX

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ABSTRACT

Male Sprague-Dawley rats were subjected to 15 minutes of temporal unilateral common carotid artery occlusion and up to 6 hours of recirculation was empolyeed. The Lt cortical concentration of Noradrenalin (NA) and its metabolites Vainyllmandelic acid (VMA) were determined by High Performance Liquid Chromatography with electrochemical detection. Decrease of NA and accumulation of VMA in ischemic cortex were detected. No significant change in control cortex were detected. This findings strongly suggest that postischemia increase release and turnover of catecholamine, which may explain delayed postischemic hypoperfusion was caused by postischemic vasoconstriction.

Key words : noradrenalin, vainyllmandelic acid

INTRODUCTION

Patient with stroke often deteriorate while being observed hour or even days after the initial ictus. Delayed deterioration could be prevented if the responsible pathologic processes were understood. Release of vasoactive amines, formation of vasoactive products of arachidonic acid metabolism, and disturbance of calcium ion homeostasis in cerebrovascular smooth muscle may attribute to postischemic vasoconstriction[1]. During the past decade, there has been a surge of interest in the possible relationship between brain monoamine and ischemic brain insults. Monoamine transmitters may play an important role in postischemic cerebral dysfunction. Monoamine may regulate cerebral reperfusion after ischemic insult and influence the recovery of brain ischemia. Such information would be useful in understanding the natural history of cerebral infarction and other neurovascular diseases:fruthermore, it might suggest new thera-

pies for treating the acute and chronic sequelae of such diseases.

The purpose of the this investigation was to examine the change of Noradrenaline (NA) and its metabolites vainyllmandelic acid (VMA) in ischemia.If NA do attribute the morbidity of postischemic cercbral dysfunction, such change should be evidence at this time.

MATERIALS AND METHODS

Male Sprague-Dawley rats weighting 250-300 gm were used. Animals were caged (three per cage) at constant temperatrue (about 27′) in simulated day and night condition for 3 weeks prior to study and allowed free access to drinking water and chow. The eight rats were anesthesized with ketamine hydrochloride (Ketalar,100mg/kg intraperitoneally). Left common carotid artery were exposed through ventral midline incision. The artery was isolated from adjacent nerves and clipped with Sugita aneurysm clip for 15 minutes, then was released. The animals were killed by decapitation 6 hrs after transient ischemia. The head were severed, cooled in an ice bath, and the brains were removed. Another group of five rats were subjected to sham operation without clipping the left common carotid artery. The concentartion of NA and VMA of experimental and control Lt cortex were analyzed by High Performance Liquid Chromatography with electrochemical detection (HPLC, Waters).

All values obtained from this experiment are expressed mean±SEM. The significance between control and experimental data was determined by Student's test.

RESULTS

The concentration (mean±SEM) of NA in control and ischemic cortex were 684±32 (n=5) and 326±18 ng per gram (n=8) respectively ($p<0.005$). The concentrations (mean±SEM) of VMA in control and ischemic cortex were 286±16 (n=5) and 502±18 ng per gram (n=8) respectively ($p<0.005$). The differences were stastically significant.

DISCUSSION

In the recirculation period following cerebral ischemia, an initial reactive hyperemia is succeeded by a secondary decrease in cerebral flow (CBF), called delayed postischemic hypoperfusion[2-8]. Cerebral recovery may be hindered by poor perfusion rather than by immediate death of hypoxic nerve cells. The hyperemia may be explained by vasodilation due to tissue acidosis from lactic acid and carbon dioxide, or by a slighy increase in extracellular potassium[9]. The cause of impaired cerebral microcirculation following ischemia has been attributed to many factors. Ames and co-workers concluded that the "no-reflow phenomenon" was due to increase blood viscosity and endothelial and perivascular glial cell swelling[10]. Klatzo concluded that arterial spasm was responsible for the no-reflow phenomenon[11]. Fluoresecnt histochemical study have demonstrated biogenic monoamines (5-HT, DA, NA) in axon terminals of the cerebral cortex, to which they project from brain stem neurons. Some investigators have assigned a regulatory role in cerebral blood flow (CBF) to biogenic monoamine, and this concept has been supported by observed effects of 5-HT, DA, NA on pial vessel diameter[12]. On the basis of the vasoactive properties of 5-HT, DA, NA, they have been speculated that the increased turnover of these amines could lead to a deleterious vasoconstriction, which might cause additional cellular damage[13].

This study showed that deprivation of blood supply to the brain led to reduction of the concentration of NA in the cerebral cortex. This reduction is due to the increased release of these monoamines, since the rates of its synthesis and degradation are depressed after vascular occlusion. The concentration of VMA are increased in the brain following vascular occlusion, it is possible that VMA increased as the result of increased metabolism of biogenic monoamines release from their stores. Wurtman and Zervas have postulate that an inappropri-

ate loss of monamine neurotransmitters may exacerate the pathophysiologic changes caused by initial ischemia[14]. Reduction of biogenic monoamines concentration in cerebral cortex appeared at the time when adenosine triphosphate levels already were reduced for a long period. Unlike many other cell types, neuron in vivo appear incapable of using any other substance than glucose as their main energy source. Under normal circumstances, adenosine triphosphate, the energy source for the maintaince of the electrochemical gradients, is efficiently produced through aerobic glycolysis and oxidative phosphorylation. Cerebral ischemia which is characterized by deprivation of glucose and oxygen sypply to the brain, inevitable led to ATP depletion. Therefore, it appears that release of biogenic monoamine in the brain is most probably related to a failure of the neuronal energy stores and the membrane transport following vascular occlusion[15]. Welch, Hashi and Meyer have suggested that a fall in biogenic monoamine reflects release of transmitter 5-HT into the extracellular fluid where it may have the effect of limiting capillary perfusion by vasoconstricting small vessels[16]. The post-ischemic disruption of flow and metabolism, therefore, creates a potential theraputic intervention because it occurs at time when patient are often under medication.

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腦缺血對大鼠大腦皮質兒茶胺濃度改變之研究

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雄性大白鼠左側頸動脈以血管夾夾住15分鐘後釋放，於再循環六小時後斷頸取出其大腦，以High Performance Liquid Chromatography with Electrochemical Detection測量左、右大腦皮質Noradrenaline (NA)，及其代謝物Vainyllmandelic acid (VMA)的濃度。對照組僅做頸切開，暴露左頸總動脈，其它與實驗組相同。結果左側缺血大腦皮質NA的濃度較對照組減少，而其代謝物VMA的濃度較對照組增加。

由此實驗結果，可認爲腦缺血缺氧後Noradrenaline釋放及轉變的增加是造成腦缺血後血管收縮的原因。

關鍵詞：正腎上腺素，香草杏仁酸