LEVELS OF ZINC IN THE CEREBRAL HEMISPHERES FOLLOWING PARENTERAL PENICILLIN IN RATS

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SUMMARY: Recognition that zinc (Zn) is a convulsant and is elevated in some seizure susceptible animals prompted this study of cerebral Zn after systemic penicillin. The distribution of Zn in the brain was investigated in rats with systemic penicillin (3 million IU/kg, i.p.) and in controls. Animals were perfused intracardially 2 h after penicillin. Brain tissues were analyzed for Zn by atomic absorption spectrophotometer. In animals, receiving i.p. penicillin hemispheric Zn was slightly elevated but not significantly different from controls. The mean zinc concentration of right hemispheres was 16.37±1.45 μg/g. (wet weight) for controls and 17.74 ±1.4 μg/g for epileptics. On the other hand, the mean Zn concentration of left hemispheres was 16.93 ±1.97 μg/g for controls and 17.56 ±1.71 μg/g for epileptics. The results indicate that there seems to be no significant relationship between penicillin induced seizures and whole cerebral Zn concentrations.

Key Words: Zinc, Cerebral hemispheres, Penicillin, Epilepsy.

INTRODUCTION

Zinc is known to play an important role in synaptic transmission (1,2). Ultrastructural studies have suggested that Zn is localized to synaptic vesicles (3) where it is released into the synaptic cleft with electrical or chemical stimulation (4,5). On the other hand, there are several reports on the convulsive effects of Zn (6,7). Moreover, elevations in hippocampal Zn have now been reported for the kindling (8,9), photosensitive (10), and the audiogenic (11) models of epilepsy.

In view of mentioned data the present study was undertaken to investigate if the concentration of Zn in whole cerebral hemispheres was altered during the parenteral penicillin model of epilepsy in rats.

MATERIALS AND METHODS

30 adult male albino Wistar rats (200-250 g) were used. Experimental group was 15 rats and 15 rats served as control. Experimental animals were injected with 3 million IU/kg, i.p. penicillin C potassium, and control animals were given and identical volume of physiological saline (PS). Animals were anaesthetized with sodium pentobarbital (45 mg/kg, i.p.) and perfused with neutral formalin 2 hours after penicillin PS. Brains were removed using plastic instruments and the wet weight of the samples was recorded. The hemispheres were separated and frozen at -70°C until Zn analysis. Brain samples were dried at 100°C for 2 days and ashed in porcelain crucibles at 500°C. The ash was dissolved with 3 ml of 3N HCl and transferred quantitively to a 25 ml volumetric flask. Further dilutions were made with 0.36 N HCl. Care was taken to minimize the possibility of zinc contamination from exogenous sources.

For detection of the Zn a Perkin-Elmer Model 2280 (Flame) atomic absorption spectrophotometer was used. Zn content of samples were measured using the 213.9 nm absorption line. The significance of the hemispheric differences was tested by the Student's t test. The content of zinc in the two hemispheres were used to calculate the asymmetry coefficient given by Glick *et al.* (12): (High side/low side)-1) x 100.

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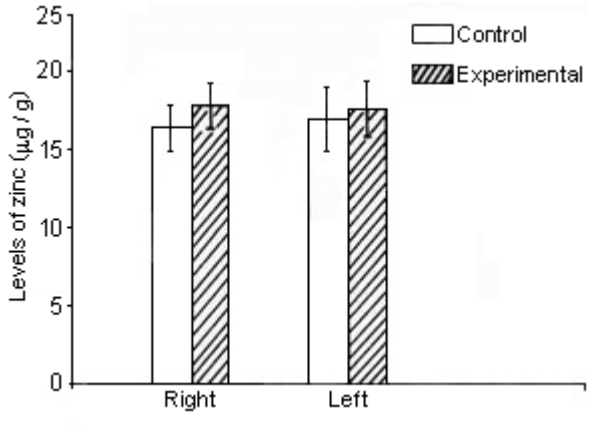

Figure 1: Marangoz *et al.* Levels of Zinc in the Cerebral Hemispheres Following Farenteral Penicillin in Rats.

RESULTS

The general behavior of the animals in the control group showed nothing abnormal during 2 h observation. The spontaneous activity of rats in the experimental group was initally, reduced after penicillin injection and there after hyperactivity. Myoclonic jerks appeared in facial muscle; subsequently, the muscle of the neck and forelimbs became extended and clonic movements appeared. Myoclonias lasted for 1-1.5 h then tended to disappear. Shortly after disappearance of myoclonias in three rats generalized clonic convulsions were started by 1 Hz clapping sound lasted about 1 min intervals, and at each time general convulsions were seen.

The zinc content in whole right and left cerebral hemispheres in the control and penicillin treated groups is presented in Figure 1. The zinc concentration was 16.37± 1.45 μg/g and 16.93 ± 1.97 μg/g (mean ±SEM) wet weight for the right and left hemispheres, respectively. The left-right difference was not significant (P>0.05).

The zinc concentrations of left (17.56 ±71 μg/g) and right (17.74±1.4 μg/g) hemispheres were slightly elevated following i.p. penicillin. Parenteral penicillin tended to elevate total zinc in the whole hemispheres, but these changes (8.37 % for right and 3.72 % for left hemispheres) were found not to be significantly different from controls. The values for zinc concentration obtained from control and experimental groups are in good agreement with other studies (8,9,13). The differences in zinc content between left and right hemispheres in both groups were significant (P>0.05).

DISCUSSION

The results of this study demonstrate only slight elevations in the content of zinc in cerebral hemispheres following systemic penicillin. A number of studies suggest an association between abnormal zinc metabolism and convulsive disorders (1,7-14). Several studies have also shown that the cortical and hippocampal zinc is markedly increased during kindling (8,9,14) or other models of epilepsy (10-13). More recently, it has been shown that the parenteral penicillin has an epileptogenic effect in rats (15,16). Possible changes in cerebral zinc level in the penicillin model of epilepsy have not previously been studied.

The convulsant effect of penicllin is thought to be due to an antagonism of gamma-aminobutyric acid (GABA) (17). On the other hand, zinc plays an important role in the synthesis, functional action and uptake velocities of GABA and glutamate (2, 18). Furthermore, according to recent data zinc blocks N-methyl-D- aspartate (NMDA) response on pyramidal neurons of the pyriform cortex (19), and cultured cortical neurons (20).

In the light of the mentioned results, it may be expected therefore, that the parenteral penicillin would cause marked elevation in cerebral zinc content. However, measurements of the total hemispheric zinc did not reveal any major changes in the content of this cation. Whether the reverse is true for an increase in zinc concentrations of some cortical and subcortical structures (e.g. hippocampus) in the penicillin model of epilepsy remains to be determined.

In conclusion, there seems to be no significant association between penicillin induced seizures and whole cerebral zinc concentrations.

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