Responses of Isolated Canine and Simian Basilar Arteries to Thiopentone by a Newly Designed Pharmacological Method for Measuring Vascular Responsiveness

T. Tsuji and S. Chiba

Department of Neurosurgery and 1 Department of Pharmacology, Shinshu University School of Medicine, Matsumoto, Japan

Summary

The stainless steel cannula inserting method was modified for application to observe vascular responses to thiopentone in the isolated basilar arteries of the dog and monkey. In the dog, thiopentone (0.01-3 mg) induced a monophasic vasoconstriction in a dose-dependent manner. On the other hand, in the monkey, thiopentone (0.01-3 mg) showed a biphasic vascular response, i.e., an initial vasoconstriction followed by a vasodilatation in a dose-dependent manner. Thiopentone usually produced much more potent vasoconstriction in the dog than that in the monkey, while potassium chloride made little difference of vasoconstriction between the dog and monkey basilar arteries. These findings suggest that thiopentone exerts a direct constrictive effect on cerebral vessels, the actions of which decrease the total cerebral blood volume and the brain bulk, allowing a reduction in intracranial pressure.

Keywords: Canine basilar artery; simian basilar artery; thiopentone; barbiturate therapy.

Introduction

It is well recognized that the control of the intracranial pressure is the most important management for the patient with intracranial hypertension. Although barbiturates have been applied to reduce the intracranial pressure19,24,27,28, the precise mechanism for barbiturates including direct cerebrovascular responses or contributions to the cerebral mechanism has not been clarified yet. The stainless steel cannula inserting method was originally developed by Hongo and Chiba12 for relatively larger arteries, and modified by Tsuji and Chiba34. In this study, we improved on this method for the purpose of measuring vascular responsiveness of cerebral arteries and made an attempt to compare the effect of thiopentone on the isolated basilar arteries of the dog with those of the monkey.

Materials and Methods

Six mongrel dogs (8-15 kg) and five Japanese monkeys (Macaca fuscata fuscata) (6-14 kg) of both sexes were anaesthetized with sodium pentobarbitone (30 mg/kg, i.v.) or ketamine hydrochloride (5 mg/kg, i.m.), respectively, and the animals were sacrificed by rapid exsanguination from the right common carotid artery after the treatment with sodium heparin (500 units/kg, i.v.). The whole brain of the animals was extirpated as soon as possible, and the rostral surface of the brain stem (5 mm in thickness), which was accompanied with the basilar artery and a lot of small branches, was resected under an operative microscope as carefully as possible. The total basilar arteries (1.0-1.5 mm in outer diameter and 1.0-3.0 cm in length) were cannulated gently and carefully under an operative microscope to avoid endothelial damage of the artery. A stainless steel cannula with 3 holes at 5 mm distance from the distal blind end (21 gauge, 0.83 mm in outer diameter and 3 cm in length and 23 gauge, 0.69 mm in outer diameter and 3 cm in length) was prepared in accordance with the inner diameter of the basilar artery in order to obtain an adequate initial perfusion pressure. One of the stainless steel cannulae, of which the outer diameter was a little thinner than the inner diameter of the basilar artery, was selected and inserted into the inner lumen of the basilar artery. The distal part of each isolated basilar artery, which was cut close to the basilar bifurcation, was tied with a thin thread to the cannula. The proximal part of the basilar artery was cut away from the vertebral arteries. Thus, the whole length of the basilar artery was cannulated with the stainless steel cannula. A plastic solid plate was attached to the dorsal surface of the specimen and bilateral sides of the specimen were clipped with 2 ultra-long clips33, which were in parallel with the basilar artery 5 mm away, in order to prevent leakage of the solution from small branches of posterior or bilateral sides of the basilar artery, which were surrounding and penetrating to the brain stem. Fig. 1 shows a diagram of the isolated basilar artery preparation. Then, the basilar artery was fixed between the surface of the brain stem and the arachnoid membrane, and a single stream of the solution flowing from the inserted stainless steel cannula ensured passage through the intra-
T. Tsuji and S. Chiba: Responses of Isolated Canine and Simian Basilar Arteries to Thiopentone

Posterior cerebral artery
Plastic plate
Brain stem
Holes of cannula
Basilar artery
Small branches from basilar artery
Vertebral artery

Injection site
Rubber tube
Sugita's Ultra-long clip

Flow

Fig. 1. Diagram of the perfused specimen inserted with a stainless steel cannula connected to the rubber tube through which the drug solution flows. The small branches from the bilateral sides of the basilar artery were obstructed with 2 Sugita's ultra-long clips at a 5 mm distance from the artery and in parallel with it. The plastic plate prevents the flow of the solution from the posterior side of the basilar artery. Arrows indicate the flow direction of the drug solution injection into the rubber tubing, closely connected to the shank of the specimen, was 0.01–0.03 ml by a microinjector (Terumo Co.) and the injection time was 4 seconds.

The data are presented as mean ± SEM in the text and illustrations. An analysis of variance with replicates was used to evaluate any differences in the responses among the groups. Drugs used were sodium thiopentone (Tanabe), and potassium chloride (Wako).

Results

a) Constrictor Responses of the Canine Basilar Artery to Thiopentone

When a relatively large dose of thiopentone (0.01–3 mg) was given intraluminally to the basilar artery of the dog in a single injection, an immediate increase in perfusion pressure was observed in all examined experiments (Fig. 2). The threshold dose for inducing a

![Fig. 2. Vasoconstrictor effects of increasing doses of thiopentone in the isolated basilar artery of the dog](image)

constriction was approximately 0.01 mg, ranging from 0.01 to 0.1 mg. The maximum increase in perfusion pressure by thiopentone was frequently over 70 mm Hg at the dose range 0.1 to 3 mg. The response to thiopentone was repetitively induced as only a monophasic vasoconstriction in a dose-dependent manner when the injection interval was longer than 5 minutes. Although the peak vasoconstrictor effect by thiopentone was transient, the change of the perfusion pressure persisted for approximately 1 minute to return to the resting level, at a dose of 3 mg of thiopentone.

b) Vascular Responses of the Simian Basilar Artery to Thiopentone

When thiopentone was administered into the simian cannulated basilar artery, initial vasoconstriction followed by vasodilatation was usually observed in a dose-related manner (Fig. 3). The threshold dose for induc-