ON THE SPECIES DIFFERENCE OF THE APPEARANCE OF BLOOD PRESSURE ACTION OF LOBELINE IN ANIMALS

SABURO HARA AND YOSHIYUKI KIKUTA

Department of Pharmacology, Tokyo Medical College, Tokyo
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INTRODUCTION

Hara and his co-workers (1-6) have been carrying out pharmacological examination of lobeline for the past 30 years. In the present series of experiments, reexaminations were made on the action of lobeline on blood pressure, especially from the point of comparative pharmacology. There are numerous reports on the action of lobeline on blood pressure, including those of S. Hara (1-3), F.R. Curtis and S. Wright (7), P. Weger (8), H. Gremels (9), W.W. Sakussow (10), and C. Heymans (11). However, their interpretation of the phenomenon differs since each observation was made on different animals, some claiming that the blood pressure decreases due to vagus nerve stimulation and others maintain that blood pressure is elevated because lobeline acts on the chemoreceptor of the aorta and carotid artery to excite the vasomotor center. Since the action on blood pressure is a summarized result of various factors, it goes without saying that no generalization of the action can be made but it was found that each of the actions of lobeline was markedly different between various animal species. The most marked was the fact that this substance causes depression of blood pressure in herbivorous animals while it caused elevation of blood pressure in carnivorous animals. This fact was confirmed again and at the same time, some examinations were made on the mechanism of the appearance of such action.

EXPERIMENTAL METHOD

Experimental animals used were guinea pigs, rabbits, dogs, and cats. Changes of blood pressure was measured at the carotid artery and observations were made by the methods described under each item. Lobeline preparation used was Lobeline Hydrochloride (Ingelheim) and administered as intravenous injection.

EXPERIMENTAL RESULT

1) Experiments in Normal Animals

In rabbits and guinea pigs, 0.5-1.0 mg/kg of lobeline caused transitory depression of blood pressure (Fig. 1), while in dogs and cats, 0.2-1.0 mg/kg of lobeline caused invariable but transitory elevation of blood pressure (Fig. 2).
FIG. 1. Action of lobeline on blood pressure. Normal rabbit

FIG. 2. Action of lobeline on blood pressure. Normal dog

FIG. 3. Action of lobeline on blood pressure. Decapitated rabbit

2) **Experiments in Spinal Animals**

Under artificial respiration after decapitation above the cervical spine, no change in blood pressure appeared in rabbits with 0.5-2.0 mg/kg of lobeline, or in dogs and cats in the same dosage, although the normal elevation of blood pressure was observed on the administration of adrenaline (Fig. 3).

3) **Experiments in Thoracotomized Animals**

In thoracotomized animals under artificial respiration, a transitory depression of the blood pressure appeared in rabbits with 0.5-1.0 mg/kg of lobeline, while elevation of blood pressure was observed in dogs and cats. This indicates that the action of lobeline on the blood pressure appears in rabbits, dogs and cats independent of respiratory excitation.

4) **Experiments in Vagus-Severed Animals**

When the vagus nerve is severed at the neck, 1.0-2.0 mg/kg of lobeline causes a slight fall in blood pressure in rabbits but is much more suppressed than at normal times. On the other hand, elevation of blood pressure as at normal times appears in dogs and cats.

5) **Experiments in Atropinized Animals**

When atropine sulfate is administered in a dose of 20-50 mg/kg by subcutaneous injection followed by the administration of 0.5-2.0 mg of lobeline after 15 minutes, there was no
fall of blood pressure in rabbits, indicating a strong suppression of the actions compared to the sole administration of lobeline. In dogs and cats, however, normal elevation of blood pressure was observed.

6) Experiments in Animals Pretreated with Ergotamine or Yohimbine

After subcutaneous injection of 0.2-0.5 mg/kg of ergotamine or yohimbine, lobeline was administered 15 minutes later and a fall of blood pressure as at normal times appeared in rabbits, while no elevation of blood pressure appeared in dogs and cats with 0.5-1.0 mg/kg of lobeline, indicating a strong suppression of the action compared to sole administration of lobeline.

7) Experiments in Animals given Electric Shock at the Hypothalamus

In accordance with the usual practice in this laboratory, an electric shock (5V × 10 cycle) was given to the hypothalamus of a rabbit and the effect of lobeline on the increased blood pressure was examined, but almost no effect was observed with a dose of 1.0-2.0 mg/kg.

8) Experiments with Carotid Artery Occlusion

Carotid arteries on both sides were closed for a time and the effect of lobeline on blood pressure was examined but practically no effect was observed with a dosage of 1.0-2.0 mg/kg, either in rabbits, dogs, or cats.

9) Experiments in Adrenalectomized Animals

With total adrenalectomized animals, a slight blood pressure fall appeared in rabbits with 0.5-1.0 mg/kg of lobeline, while no effect appeared with 0.5-2.0 mg/kg in dogs and cats. In some cases of latter animals, a slight depression of blood pressure was noticed (Fig. 4).

10) Experiments in Splenic Volume

Variations in splenic volume was observed by concurrent recording with blood pressure by the use of the improved oncometer devised in this laboratory. In rabbits, 0.5 mg/kg of lobeline caused transitory decrease in splenic volume, with fall in blood pressure. On the other hand, a transitory decrease in splenic volume is accompanied with elevation of blood pressure in cats. During the electric stimulation to preganglionic fiber of coeliac ganglion
and administration of adrenaline, decrease in splenic volume and elevation of blood pressure appeared in both rabbits and cats (Fig. 5).

**FIG. 5.** Action of lobeline on blood pressure.
Blood pressure (upper) and variation in splenic volume (lower) in a cat.

**SUMMARY AND CONSIDERATION**

In normal animals, lobeline causes fall of blood pressure in rabbits and guinea pigs and elevation of blood pressure in dogs and cats. However, these effects do not appear in the so-called spinal animals, decapitated above the cervical spine. The effect on the blood pressure is the same as at normal times in thoracotomized animals under artificial respiration. These facts suggest that the action of lobeline on blood pressure is central and is not affected by gas metabolism of the blood by respiration excitement reported by Mori (5) and Akimoto (6). Since the fall of blood pressure in rabbits caused by lobeline is markedly suppressed by the severance of vagus and by pretreatment with atropine, the action is thought to be caused by the stimulations of the vagus. There was not effect of lobeline on the blood pressure elevated by the electric stimulation of hypothalamus, or by the occlusion of carotid arteries. Therefore, it may be assumed that the action of lobeline in causing the fall of blood pressure is not directly connected with the ganglionic blocking and depressor reflex.

The elevation of blood pressure in dogs and cats caused by lobeline is suppressed by pretreatment with ergotamine or yohimbine, and the effect does not appear in adrenalectomy. On the other hand, lobeline causes contraction of the spleen, as in the case of electric stimulation on preganglionic fiber of coeliac ganglion and administration of adrenaline. Therefore, it may be considered that the elevation of blood pressure in dogs and cats is caused by increased secretion of epinephrine by the stimulation of sympathetic nerves. However, since there was a transitory contraction of the spleen in rabbits and disappearance of blood sugar-
increasing action of lobeline by adrenalectomy, reported by Tsuchiya (4), it seems that the action of lobeline is partly towards excitation of the sympathetic nerves.

The foregoing experimental results indicate that the action of lobeline on autonomic nervous system is two phasic, the one being adrenergic and the other cholinergic. In the action of lobeline on blood pressure, the former appears in carnivorous animals like dogs and cats, and the latter in herbivorous animals like rabbits and guinea pigs.

CONCLUSION

1. Lobeline effects fall of blood pressure in herbivorous animals like rabbits and guinea pigs and elevation of blood pressure in carnivorous animals like dogs and cats.

2. Lobeline has two-phasic action an autonomic nervous system, the one being cholinergic and the other adrenergic effect, and the former markedly appears in herbivorous animals and the latter in carnivorous animals when examined by change in blood pressure.

In short, the action of lobeline on the blood pressure of herbivorous and carnivorous animals is a good example that indicates the importance of comparative pharmacological observations.

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