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Effects of Histamine Receptor Blockers and the Rate of Administration of Morphine on Cardiovascular System

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Blood pressure reduction during the high dose morphine anesthesia was investigated from the point of view of histamine receptor blockers and the rate of morphine administration. It was found as the results that blood pressure reduction was prevented by the administration of the histamine receptor blockers, and the effect was almost equivalent to that caused by morphine with the rate of infusion at 2 mg/min. Safer anesthesia may be performed in term of blood pressure reduction when H_1 and H_2 receptor blockers and a slow infusion of morphine with small divided doses are given.

INTRODUCTION

A high dose morphine anesthesia is a good tool for the open heart surgery[2)7)] since it does not give serious effect on the cardiovascular system. However, blood pressure reduction is frequently observed in the early phase of anesthesia. Such reduction in the blood pressure is ascribed to the histamine release by the action of morphine[3)-6)], so that for the purpose of preventing the blood pressure reduction, slow infusion of morphine[1)3)-6)] or administration of H_1 and H_2 histamine receptor blockers should be considered.

In the present study, we investigated the effect of the rate of infusion of morphine and histamine receptor blockers on the reduction of blood pressure, in the prevention of blood pressure reduction, when a high dose morphine anesthesia was carried out in the valve replacement surgery for the mitral valve and aortic valve insufficiency.

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SUBJECTS AND METHODS

The subjects in the present study were 19 patients with ASA class II to III of the mitral valve and aortic valve insufficiency receiving the open heart surgery at the Hospital of Medical College of Oita. Group I (4 patients) was the control, Group II (5 patients) was 4 mg/kg cimetidine and 1 mg/kg diphenhydramine administered group, and Group III (10 patients) was morphine hydrochloride, by slow infusion, administered group. Prior to 45 min of entering the operating room, 0.01 mg/kg atropine, 0.1−0.2 mg/kg diazepam, and 0.1−0.2 mg/kg morphine hydrochloride were given intramusculaly to the patients.

After entering into the operating room, ECG monitor was installed to the patient together with the radial artery canulation and Swan-Ganz catheter, under local anesthesia.

To the patients in the Group II, 4 mg/kg cimetidine and 1 mg/kg diphenhydramine were administered, intravenously.

Induction of anesthesia was performed as follows: after i.v. injection of 0.3−0.4 mg/kg diazepam, and 0.12 mg/kg pancuronium, morphine was administered to the Group I and II at the rate of 2 mg/kg during 5 min, and to the Group III at the rate of 2 mg/kg for 40 to 50 min. As the supplemental fluid, 5% albumin solution was infused to 10 mg/kg during 5 min after the initiation of anesthesia in the Groups I and II, and the infusion was continued in the Group III until the end of the morphine administration.

The parameters measured for the purpose of monitoring were heart rate, blood pressure, cardiac output, systemic vascular resistance and plasma histamine levels, and the time of measurement was i) before the induction of anesthesia in the control, ii) after 10 to 15 min of induction of anesthesia in the Group I and II, and iii) after 30 to 45 min of induction of anesthesia. In the Group III, when i) the control and ii) 1 mg/kg morphine was administered, and iii) after 2 mg/kg of morphine was administered, these parameters were measured.

Histamine levels were determined by RIA method with 10 ml plasma collected with EDTA, and frozen at −20°C after plasma separation.

The obtained data were tested by the Student's t-test, and when the data showed difference with $p<0.05$, they were judged to be statistically significant.

RESULTS

1, There was no statistically significant difference among patients in age and body weight between groups.

2, There was no difference in the heart rate at any points between the groups.

3, Change in the mean blood pressure (Table 1 and Fig. 1): Marked blood pressure reduction in approx. 40% was seen in the Group I 10 to 15 min after the induction of anesthesia. Blood pressure was tend to be reduced in the Group II, but the reduction was not significant. In the Group III, blood pressure was tend to be reduced, but it

Table-1: Hemodynamic parameters and plasma histamine concentration.

Hemodynamic Parameters and Plasma Histamine Concentration

Parameters	Time / Group	1 : Control	2	3
H.R. (bpm)	I	74.3 ± 21.2	81.8 ± 28.9	80.8 ± 31.8
	II	79.2 ± 12.6	89.2 ± 17.0	67.3 ± 14.0
	III	89.2 ± 26.2	74.2 ± 18.8	65.7 ± 15.7
Mean B.P. (torr)	I	87 ± 4.7	52.3 ± 12.6*	77.5 ± 8.1
	II	91 ± 10.7	79.2 ± 15.6	84.2 ± 9.4
	III	92.7 ± 11.2	77.5 ± 7.8	80.9 ± 14
C.I. (l/m^2)	I	3.1 ± 0.8	2.7 ± 0.9	2.7 ± 0.7
	II	3.0 ± 0.7	2.5 ± 0.7	2.4 ± 0.6
	III	3.2 ± 0.6	2.6 ± 0.6	2.4 ± 0.4
S.V.R. ($dyne.sec.cm^{-5}$)	I	1669 ± 475	867 ± 264*	1475 ± 382
	II	1768 ± 478	1341 ± 449	1672 ± 308
	III	1487 ± 496	1444 ± 344	1590 ± 445
Histamine (mmg/dl)	I	0.24 ± 0.14	0.62 ± 0.30*	0.37 ± 0.16
	II	0.37 ± 0.20	1.19 ± 0.89*	0.37 ± 0.10
	III	0.43 ± 0.17	0.59 ± 0.38	0.47 ± 0.20

Mean ± SD * P<0.05 compared to control

H. R.: Heart rate, Mean B. P.: mean blood pressure,
C. I.: Cardiac index, S. V. R.: Systemic vascular resistance,

was not significant when 1 mg/kg morphine was administered, and then no blood pressure reduction was observed until the end of administration.

4, Cardiac index: Cardiac index was tend to be lower in all groups after the induction of anesthesia as compared to the control, but the change was not significant.

5, Systemic vascular resistance (Fig. 2): Marked reduction in the systemic vascular resistance was observed in the Group I 10 to 15 min after the induction of anesthesia. but it was recovered to the degree in the control after 30 to 45 min. There was no significant change in the Groups II and III.

6, Plasma histamine level (Fig. 3): Significant increase in histamine level in the Groups I and II, as compared to that in the control group, was observed 10 to 15 min after the induction of anesthesia, but it was reduced to the level in the control after 30 to 45 min. No significant increase in plasma histamine level at any moment was observed in the Group III. However, there was no significant difference among the groups.

7, There was no complication of bradycardia, hypotension, etc. with the administration of cimetidine and diphenhydramine.

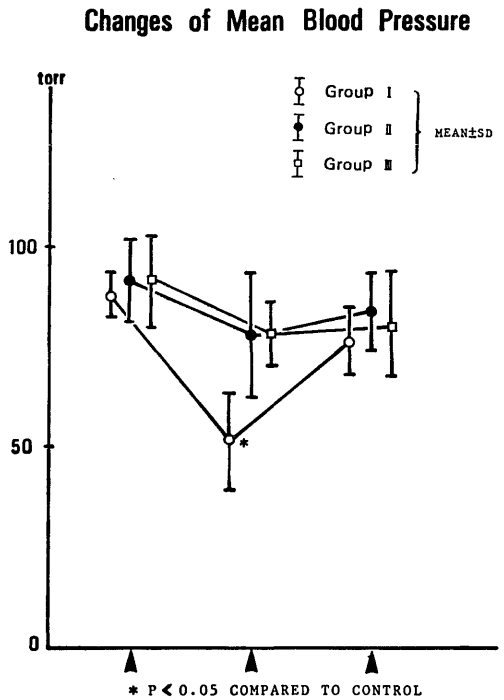

Fig. 1: Changes of mean blood pressure.

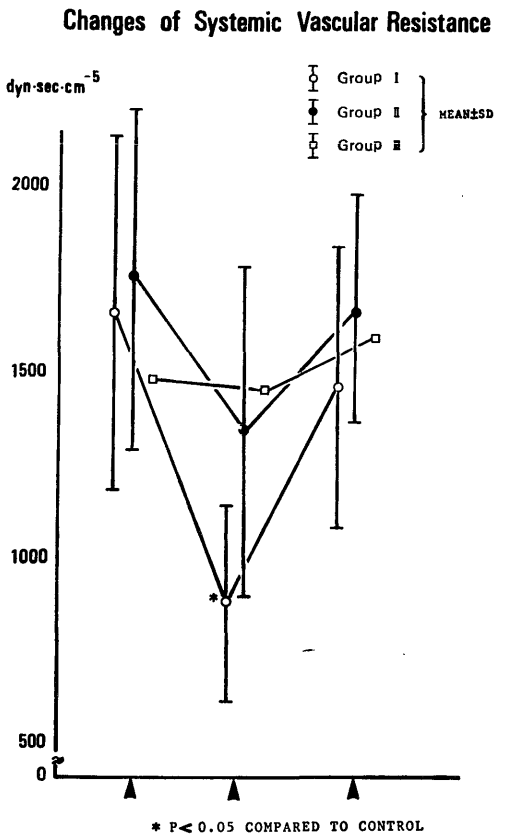

Fig. 2: Changes of systemic vascular resistance.

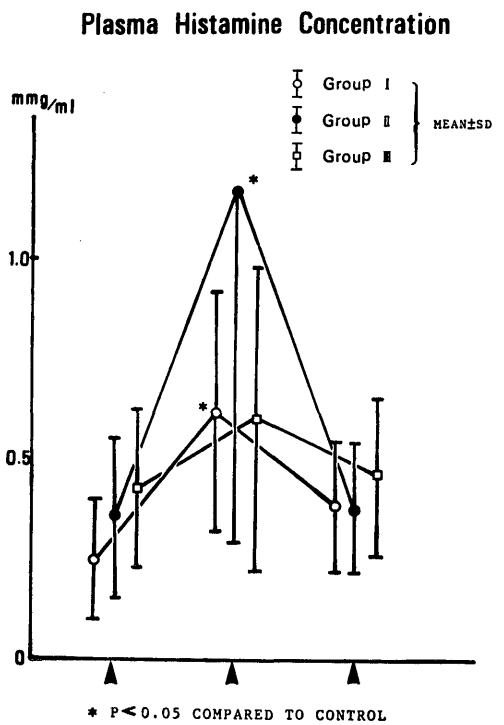

Fig. 3: Changes of plasma histamine concentration.

DISCUSSION

Changes in the cardiovascular systems, when a high dose morphine is administered, [1)3)4)5)8)] are frequently reported in the patient with heart disease, but hypotentional effect by anesthetic agent is said to be less caused. According to CONAHAN *et al.*[1)], a high dose morphine, 2 mg/kg, caused blood pressure reduction to lower than 70 mmHg of the maximum pressure in 6 cases out of 61 cases. Such reduction in blood pressure caused by the anesthetic agent has been said to be correlated with increase in plasma histamine level[3)6)], and the blood pressure reduction by the anesthetic agent can be prevented by the administration of H_1 and H_2 histamine receptor blockers[3)-6)]. We have reported the usefulness of the H_1 and H_2 histamine receptor blockers in the prevention of blood pressure reduction during the surgical operation of the acquired valvular heart disease under morphine anesthesia[4)].

However, we did not report on the rate of administration of morphine , so that it was investigated in the present study, and the following results were observed.

Histamine release is reported to be dependent largely on the rate of morphine injection, and it was confirmed in the present study that rapid infusion of morpine, as in the Group I and II, caused significant increase in the plasma histamine level, but the plasma histamine level was not significantly changed in the Group III, in which morphine administration was given slowly.

Marked lowering of the blood pressure and systemic vascular resistance as seen in the Group I was ascribed to the increase in the release of plasma histamine as reported in the literature.

In the Group III, increase in the plasma histamine level was less than in the Groups I and II, and reduction in the blood pressure and systemic vascular resistance was not significant. The fact may reflect that histamine release due to morphine was dependent on the rate of morphine infusion, and marked release of histamine was not caused by the rate, 2 mg/min.

There was no significant difference in the hemodynamic changes in the Group III from the Group II in which H_1 and H_2 histamine receptor blockers were used. Change in blood pressure was similar in these groups. Thus, it is evident that the effect of slow rate of administration of morphine is similar to the effect of histamine receptor blockers. However, from a practical viewpoint of anesthesia, small amount of morphine should be administered for the purpose of safety, not solely dependent on the administration of histamine receptor blockers. Plasma histamine levels were compared among these 3 groups. It was found that the degree of increase of histamine level in the Groups I and III was different but the difference was not statistically significant. On the other hand, marked differences in blood pressure and systemic vascular resistance were observed.

The cause might be related to numbers of cases and time of measurements.

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