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USE OF ACEBUTOLOL FOR STABILIZATION OF CIRCULATORY DYNAMICS FOLLOWING CRUSH INTUBATION

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Abstract

Effect of premedication with acebutolol (0.5±0.1 mg/kg) on the circulatory dynamics was studied compared with that with propranolol (0.05±0.01 mg/kg) and with no drug in patients in whom crush endotracheal intubation was carried out under light thiamylal anesthesia. The premedication with acebutolol avoided definitely the increase in heart rate following laryngoscopy and endotracheal intubation but not with propranolol. However either acebutolol or propranolol could not avoid the increase in blood pressure as much as that without beta blocker premedication.

ED_{50} of acebutolol which could suppress the increase in heart rate was estimated 0.3 mg/kg under such condition. No adverse effect of acebutolol was observed in this series.

The above data suggest that subclinical dose of acebutolol can be used to reduce cardiac load and to prevent provocation of latent cardiac failure following endotracheal intubation.

INTRODUCTION

Tachycardia is most often seen while endotracheal intubation is done under light general anesthesia. It persists usually for 5-15 minutes and recovers without any complication. However it is not entirely uncommon that concealed myocardial infarction or cardiac decompensation manifests following such circulatory change. We have experienced 7 cases in whom myocardial infarction developed acutely following general anesthesia for the past 7 years. In 2 cases out of them the incidence of myocardial infarction was triggered most likely by endotracheal intubation. Thus a great effort should be offered to avoid occurrence of the tachycardia. In 1960 DeVault *et al.*[1] administered phentolamine before endotracheal intubation and prevented the occurrence of tachy-

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cardia and hypertension. It is more rational, however, to use adrenergic beta blocker rather than adrenergic alpha blocker. Nevertheless it will be cautious to medicate such agent before endotracheal intubation, since most adrenergic beta blockers have bronchoconstricting potency as much as cardiac negative inotropic and negative chronotropic action. Fortunately it has successed to synthetize a new beta blocker, such as practolol or acebutolol, which affects less on bronchial muscle. Although an identical cardioselectivity is revealed in practolol and acebutolol[2,3,4,5], some incidences of skin eruption and corneal ulceration have been reported in clinical experience on use of practolol[6,7].

In this study we attempted to determine an efficacy of pretreatment with acebutolol compared with propranolol on the changes in heart rate following endotracheal intubation.

METHOD AND PROCEDURE

Study I: Forty five patients (19 males and 26 females) who aged in 19-77 and were performed surgical operation under general anesthesia in Kawasaki Medical School Hospital were subjected in this series. They were medicated with 0.5 mg of atropine and 50 mg of hydroxyzine intramuscularly in their ward at 30 minutes before induction of anesthesia. Then they were divided into 3 groups randomly as follows:

1) 15 patients without additional medication (C group)
2) 15 patients in whom 25 mg of acebutolol was given intravenously at 3 minutes before induction of anesthesia (A group)
3) 15 patients in whom 2.5 mg of propranolol was given intravenously at 3 minutes before induction of anesthesia (P group).

General anesthesia was induced by intravenous administration of 3.0 mg/kg of thiamylal sodium and an adjustable sized and cuffed endotracheal tube was inserted assisted with 1 mg/kg of succinylcholine. Subsequently anesthesia was maintained by nitrous oxide and oxygen (5:2 l/min) and respiratory control was done manually by intermittent positive pressure ventilation. In the mean time electrocardiogram by standard II lead was monitored continuously. Arterial blood pressure of the right brachial artery and heart rate were determined by Korotkow's sound auscultation and counting R wave on oscilloscope, respectively. The determination was repeated at 2 minutes before and after administration of beta blockers, during endotrachel intubation and then in every one minute until 15 minutes after intubation. Cardiac output were estimated approximately by Starr's formula[8].

Study II: Fifty patients (18 males and 32 females) who aged in 21-77 and were performed surgical operation under general anesthesia, were divided into the followed 4 groups.

1) no acebutolol medicated (15 patients).
2) 0.25-0.35 mg/kg of acebutolol given at 3 minutes before intubation (10 patients).
3) 0.35-0.45 mg/kg of acebutolol given (10 patients).
4) 0.45-0.75 mg/kg of acebutolol given (15 patients).

Premedication, induction of anesthesia and determinations of circulatory parameters were done in the same fashion as those of the first study. Statistial analysis was done by Studen's t test or paired t test.

RESULTS

In the first study, cardiac arrhythmias were occurred in 2 patients in the C group. One of them was multifocal ventricular premature beats and the other was bigeminal ventricular premature beats. Both were treated with intravenous administration of 25 mg of acebutolol. These 2 cases were eliminated from analysis. Data obtained in this series are summarized in the Table 1. Heart rate in the C group increased to 123 ± 19 beats/min sharply and significantly following intubation, as shown in the Fig. 1. Then it decreased to 96 ± 15 beats/min for the subsequent 15 minutes gradually. On the other hand, heart rate tended to increase from 79 ± 11 beats/min to 98 ± 15 beats/min after intubation in the A group. This change differed definitely from that in the C group ($p < 0.01$). Later it decreased to 93 ± 13 beats/min within 15 minutes. In the P group, heart rate increased significantly immediately after intubation. Namely it increased from 73 ± 16 beats/min to 101 ± 24 beats/min. This change was mostly identical compared with that in the C group. However subsequently the heart rate descreased to the initial level within 5 minutes in the P group. Brachial artery pressure increased immediately after intubation, namely to 187 ± 41 mmHg in the C group, 174 ± 22 mmHg in the A group and 187 ± 25 mmHg in the P group. It decreased sharply within the subsequent 5 minutes in either group and finally reached to the mostly identical level with the initial.

Changes in estimated cardiac output were also mostly comparable in those groups. Nevertheless a tendency to decrease was slightly observed in the A and P group.

In the second study, a mode of response of heart rate was evaluated

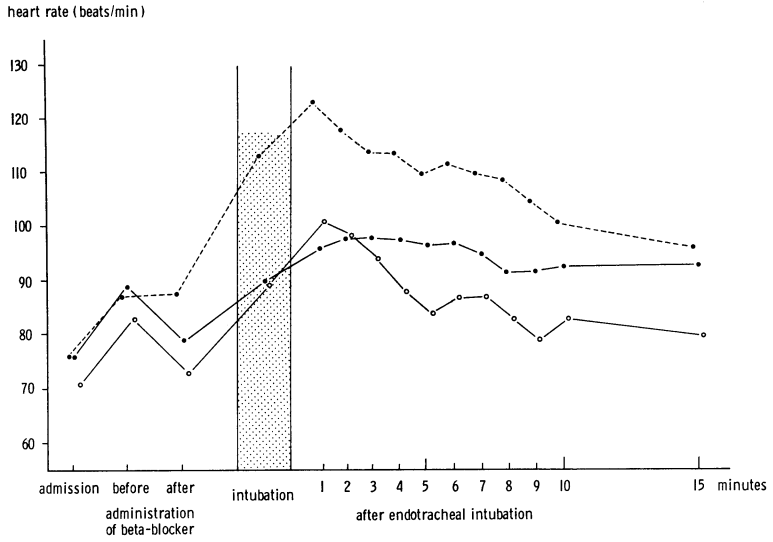

Fig. 1. Changes in heart rate before and after induction of anesthesia and intubation in the C group (•·····•), A group (•———•) and P group (○———○).

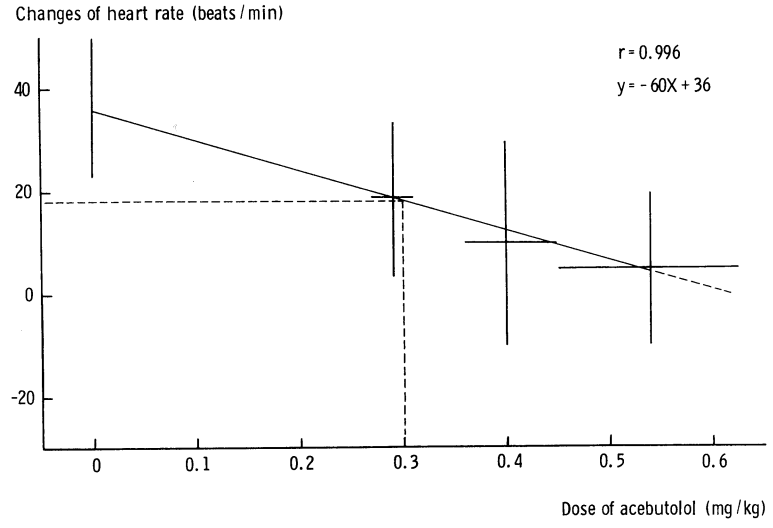

Fig. 2. Dose response curve of acebutolol on changes in heart rate.

in patients pretreated with various doses of acebutolol. Namely heart rate at 1 minute after intubation increased 36±14 beats/min from that just before induction of anesthesia in the no acebutolol medicated group. However heart rate increased 19±15 beats/min in the group pretreated with 0.29±0.02 mg/kg, 11±20 beats/min in the group with 0.40±0.04 mg/kg and 5±15 beats/min in the group with 0.45±0.09 mg/kg. A regresion line for the dose response of acebutolol, $Y=-60x+36$, was calculated from these 4 points as shown in the Fig. 2. According to these data, 0.3 mg/kg was estimated as ED_{50} of acebutolol which could suppress the increase in heart rate caused by endotracheal intubation under light thiamylal anesthesia.

DISCUSSION

Tachycardia, occasionally dysrhythmia, will occur very often associating with hypertension while laryngoscopy and endotracheal intubation is done under general anesthesia, particularly in light anesthetic level. To avoid such circulatory disturbance, several efforts had been done, such as deepening anesthetic level, application of topical anesthesia on the surface of pharynx, larynx and trachea, or superior laryngeal nerve block. None of them, however, has could prevent occurrence of the circulatory disturbance satisfactorily. Since the circulatory disturbance has been revealed to be mediated by excitation of sympathoadrenal system [9,10,11], one may use some of adrenergic beta blocker for its avoidance.

DeValut *et al.*[1] medicated adult patients with 5 mg of phenotoamine and carried out endotracheal intubation under light thiamylal anethesia. This resulted in no change in heart rate and systemic arterial pressure during laryngoscopy and intubation, although a difinite increase was observed in other patients premedicated with atropine alone. Jenkins[12] used practolol for the same purpose during bronchoscopy under light thiopental anesthesia with insufflating controlled ventilation. Desirable control of heart rate and regularity were achieved in every case. Prys-Roberts *et al.*[13] gave 0.4 mg/kg of practolol in hypertensive patients under thiopental (or althesin) anesthesia and then performed endotracheal intubation assisted with intravenous administration of succinylcholine. No noticeable changes were observed in heart rate, systemic arterial pressure and cardiac output. A similar study has been reported upon medication for YB-2 (beta blocker) before endotracheal intubation by Kim *et al*[14]. In our study, pretreatment with 25 mg of acebutolol avoided difinitely the increase in heart rate following endotracheal in-

tubation in adult patients but not with 2.5 mg of propranolol, although the increase in the latter group recovered very soon to the initial level. On the other hand, arterial pressure increased identically in either the control, acebutolol or propranolol group. Our study demonstrated that the application of beta blockers could avoid tachycardia but not hypertension. It is obvious that these agents do not produce vasodilation but also, with medication of a small dose, manifest rather positive inotropism. Nevertheless it is not always recognized that such hypertension accompanied with bradycardia does effect deleteriously on the heart. Since in the above situation coronary perfusion would be maintained fairly well and greater stress would not be loaded on myocardium. Incidentally cardiac output was estimated slightly decreased in the beta blocker treated group. On the other hand, usually beta blocker constricts bronchial muscle. Therefore someone would hesitate to use beta blocker in asthmatic patients or patients who would intubated under thiamylal anesthesia. Jenkins[12] used propranolol in few subjects at first. However he was discouraged by incidence of severe increase of air way resistance. Practolol and acebutolol have been evaluated as a most cardio-selective (less bronchoconstrictive and greater negative chronotropic) agent among many available beta blockers. Throughout our clinical study an incidence of bronchial wheezing or bronchospasm was noted in none of the subjects. Incidentally air way resistance determined before and after intubation remained unchanged in the other series of patients pretreated with acebutolol although it increased slightly and definitely with propranolol.

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TABLE 1.

Changes in heart rate, blood pressure and cardiac output in the C, A and P group (abbriviation: see in the text)

	group	admission	administration of beta blocker before	administration of beta blocker after	intubation	after intubation 1 min.	2	3	4	5	6	7	8	9	10	15
heart rate (beats/min)	C	76 ±11	87 ±20	88 ±11	113 ±22	123 ±9	118 ±12	114 ±6	114 ±14	110 ±14	112 ±11	110 ±9	109 ±10	105 ±11	101 ±12	96 ±15
	A	76 ±10	89 ±18	79 ±11	90 ±12	96 ±14	98 ±15	98 ±15	98 ±16	97 ±17	97 ±15	95 ±15	92 ±12	92 ±14	93 ±13	93 ±13
	P	71 ±12	83 ±28	73 ±16	89 ±18	101 ±24	98 ±21	94 ±21	88 ±16	84 ±17	87 ±20	87 ±20	83 ±21	79 ±19	83 ±21	79 ±19
systolic pressure of brachial artery (mmHg)	C	125 ±26	134 ±26	129 ±24	187 ±41	187 ±41	179 ±47	166 ±60	152 ±50	137 ±46	139 ±43	136 ±41	134 ±35	131 ±35	127 ±33	124 ±28
	A	124 ±15	139 ±21	128 ±15	167 ±28	174 ±22	168 ±27	158 ±30	150 ±29	145 ±29	144 ±28	138 ±28	138 ±32	131 ±30	126 ±21	126 ±21
	P	135 ±20	142 ±23	137 ±22	176 ±30	187 ±25	181 ±22	174 ±28	167 ±23	154 ±25	142 ±25	137 ±22	136 ±21	131 ±18	126 ±20	120 ±17
changes in cardiac output (1/min)	C		0	−0.36 ±1.24	−0.68 ±2.08	−0.11 ±2.24	—	—	—	−0.25 ±1.29	—	—	—	—	−0.58 ±1.24	−0.44 ±1.07
	A		0	−0.38 ±0.81	−1.44 ±0.98	−1.07 ±0.97	—	—	—	−0.80 ±0.90	—	—	—	—	−0.59 ±0.95	−0.52 ±0.87
	P		0	−0.29 ±0.49	−1.50 ±1.28	−1.13 ±1.46	—	—	—	−1.10 ±0.86	—	—	—	—	−0.67 ±0.90	−0.76 ±0.94