CHANGES IN THE HEART RATE AFTER PROCAINE

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In studying "the inhibitory action of procaine upon the reflex-bradycardia*," it was found to be necessary to make more detailed observation on the changes in the heart rate after procaine itself. Krause(1) reported recently that novocaine injected intravenously on dogs usually produced an increase of heart rate with a rise of blood pressure which continued from 2 to 15 minutes. The author's results on cats however did not fully agree with him. The heart rate was sometimes increased and at other times decreased. The mode of the change seemed to vary largely according to either the dose of procaine or the individual of the cat, and the present study was undertaken previously.

METHODS

Fourteen cats (from 2 to 4 kg in weight) anesthetized with 0.8-1 g/kg of urethane were used, and a 10 % solution of procaine hydrochloride was prepared. The necessary dose of the drug was diluted with 0.9 % NaCl solution to the amount of 1 cc and injected slowly into the femoral vein in about 1-1 1/2 minutes.

Effects on the blood pressure and the heart rate were measured at the tracing with a mercury manometer from the femoral artery. The respiration was also recorded with a tambour from the cannulated trachea.

RESULTS

1) Changes of the heart rate in course of time after procaine

The heart rate of the cat showed various changes in about half an hour after injection as shown in Table 1. However, these cases can be classified into the following four types.

a) The heart rate increases immediately after procaine, thereafter turns into bradycardia about 5 minutes later and returns gradually to the normal in 20-30 minutes.— See case No. 5,8,9,10,12,13(5mg/kg); 1,6,8,9.(10mg/kg); 14(15mg/kg).

*See this journal

b) The heart rate decreases minute by minute after injection and begins to recover about 5-10 minutes later.—*See* No. 3,4(5mg/kg); 2,3,11,12 (10mg/kg); 8,9,11 (15mg/kg).

c) The heart rate shows a continuous increase during more than 30 minutes.—*See* No. 11(5mg/kg); 7,10(10mg/kg).

d) The heart rate decreases gradually after procaine and does not recover.—*See* No. 7(5mg/kg); 4,13(10mg/kg); 5(15mg/kg).

TABLE 1. Heart rate change after procaine (intact cats)

Dose of proc.	Case No.	Before proc inj.	30 sec. after proc.	1 min.	3 - 4 min.	5 - 6 min.	7 - 10 min.	15-30 min.
5 mg/kg	3	150	138	132	130	130	138	144
	4	150	150	145	141	130	120	130
	5	160	160	160	170	165	150	153
	7	160	150	150	140	140	140	140
	8	180	190	186	180	170	160	155
	9	124	138	138	120	120	120	122
	10	126	142	140	130	123	126	126
	11	168	168	168	168	170	174	180
	12	156	156	156	126	126	126	145
	12	152	132	140	144	144	144	144
	13	102	108	102	102	104	—	—
10 mg/kg	1	150	170	180	150	135	130	120
	1	114	126	132	132	130	126	126
	2	110	105	105	105	105	105	110
	3	174	135	125	120	120	120	145
	4	204	185	180	170	—	150	150
	6	159	198	186	153	147	150	150
	7	135	140	150	145	145	150	160
	8	147	160	156	150	146	138	140
	9	122	138	138	120	120	126	130
	10	129	120	124	129	132	138	147
	11	180	159	162	162	168	170	182
	12	192	168	150	125	120	120	144
	13	123	123	120	120	120	120	102
15 mg/kg	5	201	198	192	168	162	168	160
	8	140	110	115	115	120	126	126
	9	130	120	—	110	112	120	135
	11	216	174	156	153	158	165	163
	14	180	196	190	178	170	165	176

Generally speaking, the heart rate tends to increase in smaller doses (5-10mg/kg) but tends to decrease in larger doses (15 mg/kg). It is remarkable that the change in the heart rate is always similar in the same individual. That is to

say, repeated injection of 5-10 mg/kg of procaine into the same cat at enough long intervals (40-60 minutes) causes usually the same process of the change in the heart rate. But, the administration of procaine repeated more than three or four times usually lowers the blood pressure and decreases the heart rate.

2) Influence of vagotomy on procaine actions

The series of the above experiment were all performed in intact cats. Now, these cats are injected with 5-15 mg/kg of procaine after the both vagosympathetic trunks are sectioned at the neck, then the heart rate decreases in 12 out of 13 cases. In some of these cases the heart rate is increased by procaine before vagotomy but, after that, it is decreased even by the same dose of procaine as shown in Table 2. The cardiac acceleration by procaine can be observed so long as the heart is normally innervated by the vagus.

TABLE 2. Heart rate change after procaine (vagotomized cats)

Dose of proc.	Case No.	Before proc. inj.	30 sec. after proc.	1 min.	3 - 4 min.	5 - 6 min.	7 - 10 min.	20 - 30 min.
5 mg/kg	5	135	135	130	120	120	120	-
	7	145	140	140	138	142	144	144
	8	135	138	138	138	138	138	132
	11	180	168	170	170	170	170	170
	12	169	156	156	156	156	156	156
10 mg/kg	4	145	126	126	130	130	-	-
	6	150	120	-	-	-	-	-
	7	142	130	130	138	145	145	145
	8	132	105	-	0+	-	-	-
	10	141	114	114	120	100	81	-
	11	172	150	145	150	150	156	164
	12	156	96#	144	144	148	150	152
15 mg/kg	11	153	135	120	120	135	144	150

Note: +: the cat died due to cardiac standstill.

#: the cat in which marked arrhythmia was observed at this stage.

Case 8 only shows an increase of the heart rate after procaine.

3) Parasympatholytic effect of procaine

Shen and Simon(2), Heim(3), Tanaka and Sakai(4) and others observed that intravenously injected procaine has a blocking effect on peripheral ends of the vagus. The author have also proved the same fact in the present experiment on 7 cats.

An efferent electrical stimulation of the vagosympathetic trunk sectioned at the neck is always followed by a marked bradycardia with a fall of the pressure, but this effect of vagal stimulation is entirely abolished for a few minutes by the previous administration of procaine. The larger the dosage of procaine, the longer

the period of the vagus blocking action. On the average this action persists for 3 to 4 minutes after 10–15 mg/kg of the drug but only for about a half minute after 5 mg/kg.

Schneller(5), De Elío(6), Frommel, Favre and Valette(7), Riesser and Herrgott(8) and Krause(1) recognized the parasympatholytic effect of procaine (or novocaine) in various organs and tissues of various animals. In the present study on 5 cats the marked bradycardia caused by 0.001–0.02 mg/kg of acetylcholine injected intravenously was successfully inhibited by 5–10 mg/kg of procaine administered beforehand. And it is noticeable that the fall of the blood pressure synchronizing with the bradycardia was not depressed by procaine. Procaine blocks the cardiac cholinergic nerves but not the vasodilative cholinergic.

FIG. 1. Parasympatholytic effect of procaine upon the heart
Cat ♀, 2.6 kg. At Ac 0.016 mg/kg of acetylcholine; at Pr 5 mg/kg of procaine, both intravenously. The bradycardia through acetylcholine disappears perfectly after procaine but the pressure fall can not be depressed. The number under the pressure tracing shows the heart rate.

DISCUSSION

There arises a question why procaine makes the heart rate frequent or slow according to the individual.

Procaine has a fourfold action on the heart. First of all, it blocks the sensory nerve of the heart as supposed by Fleckenstein. In this laboratory, Kido(9) ascertained by an oscillograph that percamine (nupercaine) injected into pericardium was followed by a disappearance of afferent impulses from the heart of the cat, and Hirose (not yet reported) observed that 10 mg/kg of procaine injected intravenously into the cat abolished the afferent cardiac impulses caused by adrenaline or strophanthin. This paralytic effect on the sensory nerve depresses the cardiac reflex and acts acceleratively upon the heart rate in cooperation with the sinortic reflex inhibition. The inhibitory influence of vagotomy on the procaine tachycardia relates mainly on the exclusion of the cardiac reflex.

The second is the vagolytic, as described in this paper, which action blocks the impulses from the vagus center upon the heart and promotes the tachycardia.

Thirdly, a sympathetic effect. Roth(10), Poulsson(11), Schaumann(12), Malorny and Orzechowski(13), MacGregor(14), and Chida(15) reported that procaine or cocaine in adequate dose stimulates sympathetic cardiac center and the pace maker in the heart, and causes cardiac acceleration.

But the last one acts in the opposite direction. Poulsson(11), Schaumann(12), MacGregor(14), Chida(15), Hazard(16), Brown and Acheson(17) observed the depressing effect of procaine, cocaine or other related local anesthetics upon the heart itself. This direct cardiac depression decelerates the heart rate and is believed to appear more markedly after relatively large dose of the drug.

It is obvious that these actions are not always equally aroused in every animal. In some cases accelerative action may be superior to decelerative, but the contrary can be seen in others. It depends on the physical condition or on the vagal and sympathetic tone and on the sensitivity of the heart to procaine etc. of the individual. The four types of the changes of the heart rate caused by procaine as indicated at the top of this article are thus induced from the different grade of each of the manifold action of procaine in different individual.

FIG. 2. Relation Between the fourfold action of procaine upon the heart rate

SUMMARY

1. An intravenous injection of 5–10 mg/kg of procaine accelerates the heart rate in more than half cases but decreases it in others. After 15 mg/kg of procaine the heart rate decreases in almost all cases. The changes of the cardiac rate after procaine were arranged into four types.

2. When the vagosympathetic trunks have been sectioned, procaine produces almost always cardiac deceleration. The procaine tachycardia can be observed only in such a heart which is normally innervated by the vagosympathetic nerves.

3. Procaine is vagolytic. It blocks the efferent cardiac effects of vagal stimulation. This vagolytic action is also an important factor in the procaine tachycardia. The parasymphatholytic effect of procaine is not seen in the blood vessels.

4. The discussion was made about the fourfold action — three accelerative and one decelerative—of procaine upon the heart rate. Aforementioned four types of changes in the cardiac rate after procaine come from the fact that the accelerative and decelerative actions are not always equally aroused in each case.

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