Coronary Sinus Rhythm Induced by Selective Use of Catecholamine in the in Situ Dog Heart

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SUMMARY

The selective administration of dopamine, norepinephrine, epinephrine and isoproterenol, into the coronary sinus region of the dog heart produced so-called coronary sinus rhythm, indicating the appearance of deep inverted P waves and frequently accompanied by an acceleration of pacemaker activity of the coronary sinus region. These effects of catecholamines were not influenced by atropine and tetrodotoxin but were blocked by propranolol. The coronary sinus rhythm was easily produced by suppression of SA nodal pacemaker activity. Coronary sinus rhythm may be readily elicited if the coronary sinus area is excited by adrenergic stimuli or if the SA node is suppressed by cholinergic excitation.

Additional Indexing Words:
Coronary sinus rhythm AV node artery Catecholamine

Coronary sinus rhythm is said to be due to the existence of a pacemaker in the region of the upper portion of the AV node extending into the coronary sinus. In 1944, Scherf demonstrated that warming of the area of the coronary sinus through the coronary sinus vein in the dog heart induced coronary sinus rhythm with inverted P waves with a normal PR interval. In 1965, Lancaster et al. reported that coronary sinus rhythm was produced experimentally in man, utilizing the bipolar pacing catheter in the orifice of the coronary sinus. Through clinical investigations, the coronary sinus rhythm is assumed to result from depression of the sino-atrial node.

In 1965, Nadeau and Amir-Jahd developed a technique of direct perfusion of the AV node artery. This artery, however, can not be precisely identified in beating hearts in situ because similar arteries branch off side by side with the AV node artery at the orifice of the coronary sinus. Because of the susceptibility of the AV node to induction of conduction block by acetylcholine (ACh), perfusion of the AV node artery could be improved in the

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beating heart when ACh is intraarterially injected into the perfusing system. The present authors have arranged the perfusion system of the terminal artery of the left circumflex artery near the coronary sinus for the perfusion of the AV node. In 7 out of 71 dogs, however, animals never responded sensitively to ACh but to catecholamines with inverted P waves which was indentified as coronary sinus rhythm. Our purpose in this study was to demonstrate and discuss the induction of coronary sinus rhythm.

**Materials and Methods**

Seven mongrel dogs of both sexes, weighing 6 to 14 K.g., were anesthetized with an intravenous injection of sodium pentobarbital, 30 mg./Kg. Artificial respiration was performed using a respirator provided with room air. The chest was opened through the 5th right intercostal space. The pericardium was cut, and a pericardial cradle was arranged to keep the heart in the normal position. A polyethylene tubing was inserted into one of the arteries branching from the coronary circumflex artery at the orifice of the coronary sinus and was supplied with blood from the femoral artery. When this artery perfused the AV node artery, a selective injection of ACh readily elicited conduction block of the AV node. In contrast, an injection of ACh directly into the perfusing system occasionally induced no effect on atrio-ventricular conduction even with such high doses as 10 to 100 μg. while arterial blood pressure decreased by systemic effect of ACh. Both vagal nerves were severed in these experiments. An electromanometer was arranged to measure systemic blood pressure. The electrocardiogram (ECG) was recorded on an electrocardiograph (Nihon Kohden ME-20-TR) at a chart speed of 1.5 or 3.0 cm./sec. The heart rate was continuously recorded by a cardiotachograph (Nihon Kohden RT-2), which was triggered by the R waves of the ECG.

Drugs used in this study were acetylcholine chloride (Daiichi), dl-norepinephrine, dl-epinephrine (Sankyo) and dopamine hydrochloride (Kyowa Hakko), propranolol (Sumitomo Chemicals), atropine sulfate and tetrodotoxin (supplied by Sankyo Central Laboratories). The volume of injection into this artery was 0.01 ml. in a period of 4 sec. by use of microinjectors.

In 3 dogs, direct perfusion of the sinus node artery was performed as previously described.

**Results**

*Coronary sinus rhythm induced by catecholamines*

The present authors observed coronary sinus rhythm induced by catecholamine in 7 out of 71 dogs. When dopamine, norepinephrine, epinephrine or isoproterenol was intraarterially given in the coronary sinus region, coronary sinus rhythm appeared with inverted P waves preceding the QRS complex and with a normal PR interval. Although the dosage for inducing coronary sinus rhythm varied from animal to animal, about 1 to 10 μg. of these catecholamines could elicit coronary sinus rhythm repetitively in the
Fig. 1. a: This experiment illustrates the lack of an effect of 10 and 100 µg of acetylcholine (ACh) on AV conduction and coronary sinus rhythm induced by 3 µg of norepinephrine given into the coronary sinus region (SBP, systemic blood pressure; HR, heart rate).

b: ECG recordings of coronary sinus rhythm induced by 3 µg of norepinephrine.

Fig. 2. Coronary sinus rhythm induced by i.a. injection of 1 µg of norepinephrine into the coronary sinus region during high level state of sinus rate.

Fig. 3. Coronary sinus rhythm induced by i.a. injection of 1 µg of norepinephrine into the coronary sinus region during a low level sinus rate.
same animal. If ACh was injected into the AV node artery at doses of 1 to 10 µg., complete AV block was usually induced. However, in these preparations, larger doses of ACh never produced any type of AV block. Fig. 1 shows that 3 µg. of norepinephrine induced an accelerated coronary sinus rhythm, while 30 or 100 µg. of ACh did not induce AV block although systemic blood pressure was strongly depressed. Figs. 2 and 3 were obtained by use of 1 µg. of norepinephrine on the coronary sinus region in typical experiments. On the lead II of ECG recordings, PR interval was entirely normal and prominent P waves were observed. In one experiment, administration of 3 µg. of norepinephrine induced coronary sinus rhythm followed by ven-

**Table I. Effects of Catecholamines on Coronary Sinus Pacemaker Activity in the Dog Heart**

<table>
<thead>
<tr>
<th>Catecholamine (µg.)</th>
<th>No. of dogs</th>
<th>Control sinus rate (beats/min.)</th>
<th>Maximal increase in coronary sinus rhythm (beats/min.)</th>
<th>Duration of coronary sinus rhythm (sec.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine 1</td>
<td>5</td>
<td>147 ± 8.6</td>
<td>153 ± 7.7</td>
<td>5 ± 5</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>139 ± 10.5</td>
<td>161 ± 12.3</td>
<td>67 ± 25</td>
</tr>
<tr>
<td>30</td>
<td>2</td>
<td>154</td>
<td>175</td>
<td>150</td>
</tr>
<tr>
<td>Norepinephrine 0.1</td>
<td>4</td>
<td>142 ± 7.5</td>
<td>150 ± 7.1</td>
<td>8 ± 8</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>139 ± 10.4</td>
<td>165 ± 2.9</td>
<td>33 ± 13.6</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>156 ± 13.3</td>
<td>175 ± 2.9</td>
<td>57 ± 12.0</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>141 ± 8.3</td>
<td>172 ± 1.6</td>
<td>87 ± 12.0</td>
</tr>
<tr>
<td>Epinephrine 0.1</td>
<td>4</td>
<td>149 ± 7.4</td>
<td>149 ± 6.6</td>
<td>7 ± 7</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>142 ± 14.2</td>
<td>174 ± 4.0</td>
<td>28 ± 10.1</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>172 ± 1.6</td>
<td>178 ± 1.6</td>
<td>60 ± 11.5</td>
</tr>
<tr>
<td>Isoproterenol 0.01</td>
<td>2</td>
<td>130</td>
<td>160</td>
<td>61</td>
</tr>
<tr>
<td>0.1</td>
<td>6</td>
<td>145 ± 8.4</td>
<td>168 ± 4.2</td>
<td>69 ± 32.3</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>163 ± 6.6</td>
<td>176 ± 6.0</td>
<td>106 ± 40.5</td>
</tr>
</tbody>
</table>

Each value is mean and standard error.
tricular fibrillation as shown in Fig. 4. Table I shows the comparison of the response to catecholamines on coronary sinus pacemaker activity.

Establishment of conditions for inducing coronary sinus rhythm

It is well known that coronary sinus rhythm was induced by suppression of pacemaker activity of the SA node.  In cases of heart rate of which was over 160 beats/min., coronary sinus rhythm was hardly induced by i.a. injection of catecholamine into the coronary sinus region. Coronary sinus rhythm, however, was induced by 1 μg. of norepinephrine when pacemaker activity of the SA node was suppressed by 1 μg. of bethanechol into the sinus node artery as shown in Fig. 5.

The apparent suppression of latent rhythmicity by a dominant cardiac pacemaker is well known. When electric pacing was performed at a higher than spontaneous sinus rate and subsequently stopped, sinus rate was gradually restored to normal rate before electric pacing. In these instances, coronary

![Figure 5](chart.png)

Fig. 5. a: Coronary sinus rhythm induced by 3 μg. of norepinephrine into the coronary sinus region (CO) during sinus deceleration induced by 1 μg. of bethanechol into the sinus node artery (SA) (SBP, systemic blood pressure; HR, heart rate).

b: ECG recordings of sinus deceleration induced by 1 μg. of bethanechol injected into the sinus node artery (SA) and coronary sinus rhythm induced by 3 μg. of norepinephrine injected into the coronary sinus region (CO).
sinus rhythm was occasionally observed. Fig. 6 shows that coronary sinus rhythm was induced after electric pacing of the right atrium. It suggested that the SA node was suppressed by dominant electric pacing and that pacemaker activity was temporarily initiated from coronary sinus region.

**Effects of atropine, tetrodotoxin and propranolol on the occurrence of coronary sinus rhythm**

The coronary sinus rhythm obtained by 1 µg. of norepinephrine was not blocked by 10 µg. of atropine or 1 to 10 µg. of tetrodotoxin given into the AV node artery. It was abolished by 1 µg. of propranolol. This blocking effect continued about 20 min.

**DISCUSSION**

The rhythm with an electrocardiogram exhibiting deeply inverted P waves in leads II and III and a normal or only slightly shortened PR interval has been designated coronary sinus rhythm. Concerning mechanisms of coronary sinus rhythm, anatomical observations have been made by many investigators. Tawara described specific fibers which enter the posterior part of the AV node from the sinus of the coronary vein. Kung described a small bundle of muscle fibers entering the AV node from the area of the coronary sinus. It is probably a remnant of the left-sided SA node. The coronary sinus area should be considered to possess a very high automaticity.

In the present experiments, it was demonstrated that coronary sinus rhythm was induced by injection of catecholamine into the coronary sinus region. Previously it was observed that inverted P waves after SA pacemaker depression were induced by injection of hypertonic solutions into the sinus
node artery. In 1951, Daines and Hecht reported that i.v. administered neosynephrine induced coronary sinus rhythm, and its rhythm could be blocked by dibenamine or atropine and could be interrupted by amyl nitrite, suggesting that vagal stimulation may influence induction of coronary sinus rhythm.

From these results, coronary sinus rhythm may occur when SA pacemaker activity is strongly suppressed especially by cholinergic mechanisms and when the coronary sinus region is stimulated by adrenergic mechanisms.

Acknowledgments

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References