Electrophysiologic Effects of Combined Autonomic Blockade in Patients with Sinus Node Disease

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SUMMARY. Thirty-two patients were studied before and after i.v. administration of 0.15-0.20 mg/kg of propranolol. Twenty-one of the 32 underwent combined autonomic blockade with the additional infusion of 0.04 mg of atropine. Twenty other patients with sinus node disease underwent electrophysiologic studies both before and after i.v. administration of 0.04 mg of atropine alone. Spontaneous cycle length, maximal corrected sinus node recovery time, sinoatrial conduction time, secondary pauses and intrinsic heart rate were measured. Secondary pauses were more common in those with abnormal intrinsic heart rates, and they did not correlate with changes in maximal corrected sinus node recovery time or sinoatrial conduction time. In patients with normal intrinsic heart rate, abnormal test measurements usually returned to normal after combined blockade (hypervagotonia); however, some patients showed a new abnormality after propranolol that was not reversible with atropine (catecholamine-dependent). Abnormal test responses in patients with abnormal intrinsic heart rate persisted or increased after combined blockade. We conclude that patients with sinus node disease may be categorized as (1) those with intrinsic sinus node disease; (2) those with normal intrinsic sinus node function but either relative hypervagotonia or catecholamine dependency; and (3) those with abnormal intrinsic sinus node function affected by vagal or catecholamine factors.

CLINICAL EVALUATION of patients with electrocardiographic evidence of sinus node dysfunction is difficult because of the interplay of intrinsic sinus node disease and autonomic nervous system tone. Jordan et al. suggested that measurement of the intrinsic heart rate might be of value for distinguishing patients with disturbances of autonomic nervous system tone from those with intrinsic sinus node dysfunction. One of the objectives of our report is to extend their observations of the relative contribution of sympathetic and vagal influences in patients with symptomatic sinus node disease.

Recently, Benditt et al. described the secondary pause (2P) phenomenon or abnormal prolongation of postspacing cycles 2-10 in patients with sinus node disease. They demonstrated that evaluation of postspacing cycles 2-10 increased the value of atrial pacing test in that patients with sinus node dysfunction may show the 2P phenomenon in the presence of normal sinus node recovery time and sinoatrial conduction time (SACT). The role of autonomic tone in unmasking or suppressing this phenomenon has not been studied in detail, and such information might clarify the mechanisms of the 2P phenomenon.

A second objective of this study is to evaluate the effects of vagolysis, β blockade and combined autonomic blockade on the 2P phenomenon.

Materials and Methods

The study group consisted of 52 patients with clinical features of sinus node dysfunction. Patients included for study were those with persistent sinus bradycardia, sinoatrial block, sinus pauses or the bradycardia-tachycardia syndrome. The pertinent clinical data are presented in tables 1 and 2.

All subjects gave informed written consent according to protocol approved by the Committees on Human Research at the University of California, San Francisco, and Duke University Medical Center.

Studies were performed in a cardiac catheterization laboratory with the patient in a nonsedated, postabsorptive state. All cardiac drugs were terminated before catheterization by an interval that exceeded three half-lives of any agent. Two multipolar electrode catheters were inserted into the right femoral vein. One catheter was positioned at the junction of the superior vena cava and high right atrium for atrial pacing and recording and the other was positioned across the tricuspid valve for recording the His bundle potential. Multiple surface leads were displayed simultaneously with those of the intracardiac ECGs on an oscilloscope and recorded on a DR-8 Electronics for Medicine recorder or an Elema Mingograf 800 recorder.

Study Protocol

After a 20-minute stabilization period, control recordings were obtained. Atrial overdrive pacing was instituted for 60 seconds at a cycle length of 100-200 msec below the spontaneous cycle length, and 10 con-
TABLE 1. Electrophysiologic Responses Before and After Atropine in Patients with Sinus Node Disease

<table>
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<tr>
<th>Pt</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>ECG findings</th>
<th>Control</th>
<th>After atropine</th>
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Values in italics represent abnormal responses.
Abbreviations: A = absent; BTS = bradytachycardia syndrome; CHF = congestive heart failure; CSNRTm = maximal corrected sinus node recovery time; P = present; SACT = sinoatrial conduction time; SAEB = sinoatrial exit block; SB = sinus bradycardia; SCL = spontaneous cycle length; CP = chaotic pattern; 2°P = secondary pauses.

secutive cycles were recorded after abrupt termination of pacing. Pacing runs were repeated with 50-60-msec decrements in paced atrial cycle length until a paced minimum cycle length of 350 msec was reached.8 Forty-five-second rest periods were allowed between each pacing run. The first postpacing cycle length (sinus node recovery time) and postpacing cycles 2-10 were determined after 1 minute of pacing at each paced cycle length, as described previously.8 Programmed atrial stimuli were then introduced during spontaneous rhythm, and the coupling interval was decreased in 10-msec decrements throughout the excitable portion of the atrial diastolic cycle until atrial refractoriness was achieved.9

These pacing studies were performed before and after i.v. administration of atropine, 0.04 mg/kg, in 20 subjects. In a separate group of 32 subjects, studies were performed before and after i.v. administration of propranolol, either 0.15 or 0.2 mg/kg. Propranolol was infused at a rate of 1 mg/min, with frequent monitoring of the heart rate and blood pressure. Combined blockade was achieved in 21 of the 32 subjects by the additional infusion of atropine, 0.04 mg/kg. The interval between propranolol and atropine administration was 18-30 minutes. In those 21 patients, pacing studies as just outlined were repeated 2 minutes after atropine.

Data Analysis and Criteria for Abnormal Pacing Responses

SACT was determined by the method of Strauss et al.8,10 In the absence of drugs, the upper limit of the normal range for total antegrade and retrograde conduction in our laboratories is 206 msec.11 A chaotic return pattern12,13 in the absence of marked sinus arrhythmia was considered abnormal. Mean spontaneous cycle length was determined from 20 consecutive cycles before and after each intervention. The maximal sinus node recovery times determined from the multiple pacing runs were used for data analysis. Postspacing cycle lengths 2-10 were normalized by the spontaneous cycle length and 2°Ps were defined according to criteria reported by Benditt et al.8 The first postpacing cycle was considered abnormally prolonged if the maximal corrected sinus node recovery time (CSNRTm) exceeded 525 msec.14 This value was used to compare our results with those of other studies.
of patients with normal sinus node function\textsuperscript{15, 16} given i.v. atropine or propranolol. Abnormal changes of SACT or CSNRT\textsubscript{m} after either atropine or propranolol in subjects without sinus node dysfunction were defined according to the criteria of Dhingra et al.\textsuperscript{14} and Vasquez et al.\textsuperscript{18} Values > 350 msec for CSNRT\textsubscript{m} and > 180 msec for SACT exceeded the mean ± 2 SD in a group of patients without sinus node disease who had received i.v. atropine.\textsuperscript{18} Values > 514 msec for CSNRT\textsubscript{m} and > 264 msec for SACT exceeded the mean ± 2 SD in a group of patients without sinus node disease who had received i.v. propranolol.\textsuperscript{18} The observed heart rates after combined blockade (intrinsic heart rate) were compared with those predicted from normal subjects using the formula of Frick et al.\textsuperscript{17} (predicted intrinsic heart rate = 120 − [0.58 + age] ± 8.1). We used this formula, rather than the one used by Jose and Collison,\textsuperscript{18} because it contained more subjects in the same age range as our patient population. The intrinsic heart rate was considered abnormal if it fell below 2 standard deviations from the predicted value. The data are expressed as mean ± SD unless otherwise specified. Differences were evaluated using the \textit{t} test.

\section*{Results}

\subsection*{Patient Classification}

The patients given i.v. atropine (table 1) or propranolol (table 2) were further subdivided on the basis of the predominant electrophysiologic abnormalities. These groupings included chronic sinus bradycardia, sinus pauses or sinoatrial exit block and bradycardia-tachycardia syndrome. The incidence of abnormal responses was compared among these three groups. Spontaneous cycle length was significantly longer in patients in the sinus bradycardia group (1086 ± 204 msec) compared with those with predominant sinoatrial pauses or exit block, 902 ± 146 msec (\textit{p} < 0.05), or those with the bradycardia-tachycardia syndrome, 928 ± 186 msec (\textit{p} < 0.05). There was no significant difference in the incidence of any specific abnormal test response among the groups. However, patients with bradycardia-tachycardia syndrome had a higher composite abnormal test response, 1.2 ± 0.7 abnormal responses/patient, than the sinus bradycardia group, 0.6 ± 0.9 abnormal responses/patient (\textit{p} < 0.05).

\section*{Effects of Autonomic Blockade on Secondary Pauses}

\subsection*{Effects of Atropine}

Twenty patients were studied before and after administration of atropine, 0.04 mg/kg (table 1). For the group as a whole, mean spontaneous cycle length decreased from 973 ± 227 msec to 746 ± 198 msec (\textit{p} < 0.01) after atropine. The CSNRT\textsubscript{m} was abnormal in six of the 20 patients. After atropine, CSNRT\textsubscript{m} became abnormal in two more patients, nos. 14 and 20. Control SACT was abnormal in eight of 19 (it could not be measured in one) and decreased to within normal limits in four of the eight after atropine. No patients developed abnormal values for SACT after drug administration. The changes in incidence of abnormal CSNRT\textsubscript{m} or SACT after atropine were not statistically significant. Secondary pauses were present in 13 of 20 patients under control conditions and disappeared after atropine in eight of 13, so 2°P were present only in five of 20 patients after the drug. The decrease in incidence of 2°P after atropine was statistically significant (\textit{p} < 0.02). Therefore, although atropine resulted in a decreased incidence of 2°P, associated changes in CSNRT\textsubscript{m} and SACT were variable.

\subsection*{Effects of Propranolol}

Thirty-two patients were studied before and after i.v. infusion of propranolol, 0.15 or 0.2 mg/kg (table 2). The CSNRT\textsubscript{m} during control conditions was abnormal in six of 32 patients; after propranolol, it was abnormal in nine of 32 patients; CSNRT\textsubscript{m} became normal in one and abnormal in four other patients. The SACT measured under control conditions was abnormal in 14 of 31 patients (not measured in one). After propranolol, 13 of 31 had abnormal values; SACT became normal in four and abnormal in three more patients. Thirteen of 32 patients had 2°P during control conditions. After propranolol, 15 of 32 patients had 2°P; 2°P was abolished in two and appeared in five additional patients.

For the group as a whole, the incidence of 2°P did not change significantly after propranolol, nor did the changes in 2°P correlate with changes in CSNRT\textsubscript{m} or SACT.

\subsection*{Effects of Combined Blockade}

The electrophysiologic effects of combined blockade were assessed in 21 patients (table 2). For the group as a whole, mean spontaneous cycle length (999 ± 167 msec) did not change significantly after combined blockade (962 ± 98 msec). The control CSNRT\textsubscript{m} was abnormal in seven of 21 patients. After combined blockade, abnormal values of CSNRT\textsubscript{m} were present in 10 of 21 patients; it became normal in two and abnormal in five. SACT was measured in 18 patients before and after combined blockade. Control SACT was abnormal in eight and remained abnormal in five after propranolol and in four after combined blockade. Seven of 21 patients had 2°P under control conditions; after combined blockade, 2°P disappeared in three and appeared in three other patients. We found no correlation between changes in 2°P before or after combined blockade compared with changes in CSNRT\textsubscript{m} or SACT.

\subsection*{Intrinsic Heart Rates}

The 21 patients challenged with both propranolol and atropine were further subdivided on the basis of their intrinsic heart rates (table 2). Thirteen patients had normal intrinsic heart rates and eight had abnormally low intrinsic heart rates. Changes in electro-
TABLE 2. Electrophysiologic Responses Before and After Propranolol or Combined Autonomic Blockade

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>ECG findings</th>
<th>SCL (msec)</th>
<th>2tP</th>
<th>CSNRT m (msec)</th>
<th>SACT (msec)</th>
</tr>
</thead>
</table>

Normal intrinsic heart rate

1  56  F  Syncope  Pauses  813  A  197  109
2  31  F  Dizziness, syncope  Pauses  752  A  653  85
3  87  M  Dizziness, syncope  Pauses  800  A  430  116
4  68  F  Dizziness  Pauses  775  A  335  108
5  24  F  Dizziness  Pauses  1172  P  1643  211
6  85  F  Syncope, dizziness  Pauses  860  A  190  232
7  63  F  Dizziness, palpitations  BTS  1152  A  258  120
8  86  F  Syncope  BTS  1035  A  365  20
9  42  F  Palpitations  BTS  925  P  245  200
10 65  F  Angina  BTS  940  A  280  211
11 72  M  Dizziness, angina  SB  1200  A  470  134
12 79  M  Dizziness, syncope  SB  792  A  260  120
13 79  M  Syncope  SB  1065  A  105  126

Mean ± sd 945 ± 163  418 ± 394  148 ± 51

Abnormal intrinsic heart rate

14 76  M  Dizziness, syncope  Pauses  1099  P  453  211
15 44  F  Fatigue  Pauses  971  P  1251  288
16 64  F  Syncope  Pauses  850  A  350  197
17 61  M  CHF  SB, pauses  1130  A  420  200
18 71  F  Palpitations  BTS  883  P  836  CP
19 58  M  Palpitations  BTS  650  P  520  CP
20 74  M  Syncope, angina, CHF  SB  1223  A  422  153
21 65  M  Syncope  SB  1190  P  290  155

Mean ± sd 999 ± 197  568 ± 321  192 ± 33

22* 55  M  Dizziness  Pauses  981  P  479  224
23 66  F  Dizziness  Pauses  845  A  305  144
24 63  M  Dizziness  Pauses  754  A  303  CP
25 38  M  Syncope  Pauses  861  P  202  126
26 78  F  Palpitation  Pauses, BTS  1200  P  1600  308
27 64  M  Palpitation  BTS  1110  A  560  CP
28 64  M  Palpitation  BTS  850  P  480  1* SAB
29 60  F  Palpitation  BTS  943  P  270  215
30 61  M  Palpitation  BTS  1170  A  328  207
31 44  F  Palpitation  BTS  804  P  287  136
32 55  M  Dizziness, angina  SB  810  A  185  124

*Patients 22–32 received propranolol alone.
Abbreviations: IHRp = predicted intrinsic heart rate; IHRo = observed intrinsic heart rate; SAB = sinoatrial entrance block; other abbreviations as in table 1.

Physiologic values were analyzed before and after propranolol and after atropine in the 21 subjects who underwent combined blockade.

Corrected Sinus Node Recovery Time

Mean CSNRTm did not differ significantly between patients with normal and abnormal intrinsic heart rates; however, after combined blockade (table 2), mean CSNRTm (1342 ± 1117 msec) was higher in those with abnormal intrinsic heart rate than in those with normal intrinsic heart rates (287 msec, p < 0.01). Two of 13 subjects with normal intrinsic heart rates had an abnormal control CSNRTm that remained abnormal after propranolol, but normalized after com-
Table 2. (Continued)

<table>
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<tr>
<th>SCL (msec)</th>
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<th>CSNRT&lt;sub&gt;m&lt;/sub&gt; (msec)</th>
<th>SACT (msec)</th>
<th>SCL (msec)</th>
<th>2P</th>
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Combined blockade. In contrast, control CSNRT<sub>m</sub> was abnormal in three of eight with abnormal intrinsic heart rates, but one new abnormality was detected after propranolol and three new abnormalities were detected after combined blockade. Pretreatment with propranolol of patients with abnormal intrinsic heart rates was associated with lengthening of the CSNRT<sub>m</sub> after atropine. In contrast, vagolysis appeared to normalize the CSNRT<sub>m</sub> in patients with normal intrinsic heart rates.

Sinoatrial Conduction Time

Mean SACT was significantly higher in patients with abnormal intrinsic heart rates than in those with normal intrinsic heart rates during the control period (192 ± 33 vs 148 ± 51 msec) (<i>p</i> < 0.05) and after combined blockade (194 ± 36 vs 112 ± 42) (<i>p</i> < 0.001). For patients with abnormal intrinsic heart rates, control SACT was abnormal in four, and these abnormalities persisted after propranolol. SACT remained
abnormal in three and could not be measured in one of
the four after atropine. No new abnormalities in
SACT were induced after combined blockade. In sub-
jects with normal intrinsic heart rates, control SACT
was abnormal in four of 13 subjects, but normalized in
two after propranolol. After combined blockade, only
one patient had an abnormal SACT.

Secondary Pauses

The incidence of $2^\circ$P was significantly higher in pa-
patients with abnormal intrinsic heart rates compared
with those with normal intrinsic heart rates during the
control period (five of eight vs two of 13) ($p < 0.05$)
and after combined blockade (six of eight vs one of 13)
($p < 0.005$). Two patients with normal intrinsic heart
rates had $2^\circ$Ps in the control period. After
propranolol, $2^\circ$Ps disappeared in one but manifest-
in three additional subjects. After combined blockade,
only one patient had a $2^\circ$P. In contrast, five of eight
patients with abnormal intrinsic heart rates had $2^\circ$Ps;
one additional patient had $2^\circ$Ps after propranolol that
disappeared after atropine administration. Thus, $2^\circ$Ps
were common in patients with abnormal intrinsic
heart rates either before (five of eight patients) or after
combined blockade (six of eight patients). Secondary
pauses occurred less frequently in the group with nor-
mal intrinsic heart rates either before (two of 13) or
after combined blockade (one of 13 patients).

Total Test Abnormalities

Striking differences were apparent between the
groups with normal vs abnormal intrinsic heart rates.
In the 13 patients with normal intrinsic heart rates,
eight abnormal tests were recorded. After combined
blockade, only two abnormal tests were detected.
Patients with abnormal intrinsic heart rates had 11 ab-
normal test responses in eight subjects. After combined
blockade, 16 abnormal test responses were
recorded in those patients. There was no significant
difference in the incidence of total abnormal test
responses under control conditions between patients
with normal and abnormal intrinsic heart rates;
however, the incidence of abnormal total test
responses was greater in the group with abnormal in-
trinsic heart rates (eight of 16 vs two of 13) after com-
bined blockade ($p < 0.005$). Thus, combined blockade
(especially after vagolysis) tended to normalize test
responses in patients with normal intrinsic heart rates,
whereas combined blockade resulted in an increased
incidence of abnormal test responses in patients with
abnormal intrinsic heart rates.

Discussion

Secondary Pauses

Benditt et al. described abnormal prolongation of
atrial overdrive postponing cycles 2–10 as $2^\circ$Ps. The
basic mechanism of this abnormality is unknown but
may be related in part to abnormalities in
automaticity, sinoatrial conduction, intranodal block
or intranodal oscillatory potentials that fail to reach
threshold. Regardless of the underlying mecha-
nism, the effects of vagolyses and $\beta$ blockade on
$2^\circ$P are apparent in our study. Although our data
suggest a vagal and a catecholamine component in the
$2^\circ$P phenomenon, the different responses may mainly
have been caused by the presence or absence of intrin-
sic sinus node disease. We found that $2^\circ$Ps occurred
frequently in patients who had an abnormal intrinsic
heart rate and persisted or increased in frequency after
combined blockade in these patients. In contrast, only
two of 13 patients with normal intrinsic heart rates
had $2^\circ$Ps, and those abnormalities (along with other
abnormal test responses) tended to normalize after
combined blockade. Although too few patients were
studied to draw definitive conclusions, combined
blockade apparently exerted little effect on patients
with $2^\circ$Ps and intrinsic sinus node disease (i.e., those
with abnormal intrinsic heart rates). In summary,
$2^\circ$Ps appear to be predominantly an expression of
intrinsic sinus node dysfunction, but in selected patients
both a vagal and a catecholamine component
appeared to be important (table 2). We found no cor-
relation, however, between abolition or persistence of
$2^\circ$Ps with changes in either sinus node automaticity or
sinoatrial conduction.

Normal Intrinsic Heart Rates and Changes
in Specific Electrophysiologic Measurements

Our data confirm and extend the observations of
Jordan et al. Like Jordan et al., we found that abnor-
malities in CSNRT$_m$ were uniformly abolished after
combined blockade in patients with normal intrinsic
heart rate. However, the effects of combined blockade
on other measurements of sinoatrial function, as well
as the serial studies after propranolol and atropine,
led to further insights into the relationship of the
autonomic nervous system and sinus node function. In
five of the 13 subjects with normal intrinsic heart
rates, abnormalities present either during control
observations or after propranolol disappeared after
atropine. We interpret this finding as a relative hyper-
vagotonic response and suggest that the clinical
features of the sick sinus syndrome in these subjects
may have been related to vagal overreactivity. In addi-
tion, vagolysis resulted in significant decreases in both
CSNRT$_m$ and SACT in this patient subgroup.

The important effects of acetylcholine on sinus node
automaticity and refractoriness are well estab-
lished.

In contrast, two of 13 patients with normal intrinsic
heart rate still showed abnormal test responses after
combined blockade and warrant further comment. In
patient 8, abnormalities provoked by propranolol per-
sisted after vagolysis (table 2). Similarly, patient 6,
who had abnormal control SACT, had a marked in-
crease in SACT after propranolol that failed to nor-
malize after atropine. We believe these findings are
suggestive of catecholamine dependency. There is
strong evidence for an obligatory role of catech-
olamines on cardiac pacemakers. In several patients,
both a catecholamine-dependent factor and a vagal factor appeared to be operative. Whether this reflects increased end-organ sensitivity or increased release of acetylcholine from the nerve terminals is not established by this study; either would produce a beneficial response to atropine.

**Abnormal Intrinsic Heart Rates and Specific Electrophysiologic Measurements**

Like Jordan et al., we found more abnormal test responses after combined blockade in patients with abnormal than in those with normal intrinsic heart rates. Jordan et al. interpreted their findings as suggesting that those subjects with abnormal intrinsic heart rates had intrinsic sinus node disease that was relatively unaffected by perturbations in autonomic tone. However, the pattern of response after propranolol and atropine in our study suggests an important additive role of the autonomic nervous system in these patients. For example, an abnormal CSNRTm was provoked after propranolol in patients 14 and 19 and remained abnormal after atropine. We interpret this finding to be superimposed catecholamine dependency. In contrast, patients 21 and 16 had 2°P during control studies or after propranolol that were abolished after atropine. We believe that this was probably due to the additive influence of relative hypervagotonia. Somewhat more difficult to explain is the provocation of abnormal CSNRTm in patients 16, 17 and 20 only after atropine. Prior β blockade appeared to sensitize these subjects to paradoxic lengthening of the CSNRTm after atropine; the cause of this response is not known.

Our data must be interpreted in the presence of serious limitations in the methods of assessing sinus node function. The problems related to measurements of SACT have been well described elsewhere. In addition, normalization or provocation of an abnormality must be interpreted in terms of the total electrophysiologic response. For example, apparent normalization of SACT after propranolol does not necessarily suggest improved sinoatrial conduction but may occur as a result of sinus slowing or pacemaker shift. In addition, provocation of an abnormal CSNRTm after atropine does not necessarily reflect depression of automaticity but instead improved sinoatrial conduction with more effective pacemaker suppression after atrial override pacing.

In our study the same population of patients was not tested with two different protocols, so differences in patient characteristics rather than altered autonomic tone might explain our findings. This hypothesis must therefore be tested in larger patient cohorts in whom the intrinsic heart rate is known.

In conclusion, patients broadly labeled as having the sick sinus syndrome can be more accurately categorized into three broad subgroups: (1) those with normal intrinsic sinus node function but with relative hypervagotonia; (2) those with intrinsic disease whose sinus node function is affected by changes in autonomic nervous system tone; and (3) those with intrinsic sinus node dysfunction unaffected by changes in autonomic tone. This categorization could lead to more rational treatment programs for patients with sinus node dysfunction.

**References**

Gastric Dilation During Stimulation of Cardiac Sensory Receptors

U. James Johannsen, B.A., Robert Summers, M.D., and Allyn L. Mark, M.D.

SUMMARY  Gastrointestinal symptoms are more common in patients with inferoposterior myocardial infarction than in patients with anterior infarction. These symptoms are often associated with bradycardia and hypotension, which may be caused by stimulation of sensory endings in the heart. The major goals of this study were to determine if stimulation of cardiac sensory receptors (the Bezold-Jarisch reflex) in dogs produces gastric responses, and if stimulation of receptors in the inferoposterior wall of the left ventricle produces larger gastric responses than stimulation of receptors in the anterior wall.

Gastric dilation was measured from increases in volume of a gastric balloon maintained at constant distending pressure. Cardiac sensory receptors in the inferoposterior wall (circumflex coronary artery) and in the anterior wall (anterior descending artery) were stimulated separately by intracoronary injection of veratridine in chloralose-anesthetized dogs.

Intracoronary injection of veratridine produced bradycardia, hypotension and gastric dilation. Decreases in heart rate and increases in gastric volume produced by injection of veratridine into the circumflex artery were greater than those that resulted from injection into the anterior descending artery (32 ± 10 ml vs 14 ± 5 ml, respectively; p < 0.05). Flow in these two beds and the weight of myocardium perfused by each vessel were not different.

Diaphragmatic vagotomy abolished the gastric response but not the bradycardic or hypotensive response to intracoronary injection of veratridine. Intracoronary administration of lidocaine and bilateral cervical vagotomy blocked all reflex responses to intracoronary veratridine.

Stimulation of cardiac receptors with vagal afferent pathways by veratridine in the dog evokes reflex gastric and circulatory responses in anesthetized dogs. These responses are greater during stimulation of cardiac receptors in the inferoposterior wall. A similar reflex may contribute to the nausea and vomiting in the early stages of inferoposterior myocardial infarction.

NAUSEA AND VOMITING are common symptoms in patients with acute myocardial infarction. They are more common in patients with inferoposterior infarction than in those with anterior infarction.1 Ahmed et al. reported that in 62 patients with documented myocardial infarction and gastrointestinal symptoms before administration of analgesics, 69% of the patients with inferoposterior infarction reported a history of nausea and vomiting, while only 27% with anterior infarction experienced these symptoms.1 This difference could not be explained by differences in severity of pain or the presence of shock. Thus, other mechanisms must play an important role in the pathogenesis of nausea and vomiting in these patients.

The gastrointestinal symptoms in patients with inferior infarction are often associated with bradycardia.1 The high frequency of bradycardia and hypotension during inferior infarction may result from stimulation of cardiac sensory receptors that mediate cardioinhibitory and vasodepressor responses.2 These sensory receptors may be preferentially distributed in the inferoposterior wall of the left ventricle.3,4 Abrahamsson and Thorén have reported that stimulation of cardiac receptors with vagal afferents by veratridine or ischemia in anesthetized, decerebrate cats produces reflex gastric relaxation as
Electrophysiologic effects on combined autonomic blockade in patients with sinus node disease.
J M Desai, M M Scheinman, H C Strauss, B Massie and J O'Young

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