Myocardial Response to Cigarette Smoking in Normal Subjects and Patients with Coronary Disease

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The neurohumoral responses elicited by cigarette smoking1 might be expected to affect the heart in a complex manner. Nicotine, the principal pharmacologic substance in tobacco has distinct effects upon the central nervous system,2 and peripheral ganglia,3 and is capable of stimulating the release of epinephrine4 and antidiuretic hormones.5 In view of these multiple factors which may variably modify myocardial oxygen consumption, the actual effect upon oxygen uptake of the heart may become less predictable than if one variable were altered.

The difficulty in determining the influence of cigarette smoking upon the human myocardium in terms of the work involved and energy released is that the currently available method for assessing myocardial blood flow and oxygen usage in man requires the presence of a steady state. Thus, the initial acute changes and possible phasic responses become difficult to assess. In a previous study the early response to cigarette smoking was associated with enhanced myocardial blood flow in normal subjects.6 Whether a similar situation occurs after the known peripheral hemodynamic responses1 have been established and maintained is examined in this investigation. To assess the potential role of tobacco as a cause of myocardial ischemia, the response to smoking in patients with coronary artery disease has been contrasted with that occurring in control subjects.

Procedure and Methods

The eight subjects with coronary artery disease of this study had incurred an acute myocardial infarction at least 1 year previously. This diagnosis was based on the clinical course and electrocardiograms. In addition all but one experienced angina pectoris. Cardiomegaly was not found on x-ray examination and diastolic hypertension above 95 mm. Hg was absent at the time of study. Six control subjects were studied who had recovered from acute benign illnesses. All the patients were habitual smokers.

The same experimental procedure was followed in both groups. After an overnight fast, the patient was premedicated with pentobarbital, 1 Gm. The coronary sinus and right atrium were catheterized and a needle was placed in the brachial artery. Coronary blood flow was determined in the recumbent position by the nitrous oxide desaturation technic7,8 followed immediately by a Fick cardiac output.

After the resting coronary flow and systemic hemodynamic determinations the patient began cigarette inhalation at 45-second intervals. Two cigarettes of a standard nonfilter brand were consumed in about 25 minutes, so that the initial increase of pulse rate and pressure was largely maintained during the subsequent 12 minutes of nitrous oxide inhalation. Upon cessation of inhalation, cigarette smoking was resumed at the same rate and was maintained throughout the coronary blood flow sampling. Heart rate, arterial pressure, and a left ventricular lead were monitored throughout the smoking, and were relatively constant during this procedure. In the tables are shown the values during the third minute of the coronary blood flow determination.

Results

Tabulation of the data of the control group has been made in table 1 and of the coronary group in table 2. During cigarette smoking both the control and coronary groups had significant acceleration of heart rate. A uniform rise in arterial pressure was seen in the former and with one exception, in the coronary group. Further, there was a tendency
for these hemodynamic changes to be more pronounced in the coronary group. All control subjects had an increase in cardiac index as did the coronary group, except for patients L. S. and F. N. The low values before smoking in the latter group are probably accounted for by their prior loss of functioning heart muscle. A uniform increment of left ventricular work during smoking was also more pronounced in the coronary group.

The attendant changes in coronary blood flow were not significant in either group. This phenomenon, combined with an unaltered myocardial oxygen extraction, resulted in a virtually identical myocardial oxygen usage as in the control state. The value before smoking of 8.63 ml. per 100 Gm. per minute in the coronary subjects was slightly less than that found in the control subjects, and its relation to the lower cardiac index remains speculative. In view of the relevance of myocardial usage of oxygen to the symptomatology of coronary artery disease, the relationship of left ventricular work to its oxygen consumption has been expressed as a ratio. The unknown variable of left ventricular weight precludes estimation of total left heart oxygen consumption in a given subject, but the identity of weights before and during smoking permits comparison of these two measures in a given patient. The distinct increment of left ventricular work in the presence of an unchanged myocardial oxygen consumption was reflected by a rise in this ratio of similar magnitude for both groups. This disproportion was not attended by anginal symptomatology or electrocardiographic evidence of ischemia in the patients with myocardial infarction.

Discussion

The experimental conditions of this study were limited to evaluation of the sustained effects of cigarette smoking upon the myocardium of man after the peripheral hemodynamic changes had become well established. Consequently, interpretation of the data cannot be applied without reservation to the acute changes occurring immediately after

Table 1

<table>
<thead>
<tr>
<th>Myocardial</th>
<th>Oxygen consumption (ml./Gm./min.)</th>
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</thead>
<tbody>
<tr>
<td>Initial</td>
<td>Control values</td>
</tr>
<tr>
<td>Age</td>
<td>Data obtained during smoking.</td>
</tr>
<tr>
<td>Sex</td>
<td>No significant difference between control and smoking data.</td>
</tr>
</tbody>
</table>

*p values:ACP < 0.01 < 0.02 < 0.05 < 0.05 < 0.05

Circulation, Volume XXIII, March 1961
the onset of smoking, which may well be qualitatively different.9 If one assumes, however, that nicotine is the principal pharmacologic agent in tobacco smoke, then the effects of intracoronary infusion of this substance are of some interest. In the intact dog it has not been found to modify coronary blood flow when injected into the anterior descending artery, despite substantial increase in myocardial contractility.9 Left coronary perfusion with nicotine also has failed to increase flow in the atherosclerotic rabbit heart, despite cardiac acceleration and enhanced contractility.10 These studies, in which different methods of determining coronary flow have been employed, tend to reduce the possibility that these results in man represent an artifact of the nitrous oxide method.

Augmentation of coronary blood flow may usually be anticipated when there is an increase in heart rate, systemic arterial pressure, cardiac output, and left ventricular work. In this manner, the apparently greater oxygen requirement of the myocardium would be severed. Failure to find such increases of myocardial blood flow and oxygen consumption in the coronary subjects during cigarette smoking may plausibly be related to the "fixed coronary resistance" alleged to exist in such patients.11 That the abnormal coronary vasculature is not responsible becomes apparent from the similar response in the subjects without evidence of coronary disease. In view of the evidence that ventricular contraction acts to impede coronary flow within the left ventricular wall,12 the enhanced ventricular contractility as reflected by left heart work may have produced such an effect. This view is difficult to accept, since the failure of coronary flow to meet the need for greater oxygen usage should be associated with augmented oxygen extraction.
Although many of the effects of smoking and nicotine infusion mimic those of catecholamine administration, an evaluation of endogenous catechols in plasma in response to smoking too small to affect the coronary vasculature appears unlikely. On the contrary, small graded doses of catecholamine induce changes in coronary flow before increments in rate and pressure. Another humoral agent possibly released during smoking is anti-diuretic hormone. Its potent coronary vasoconstrictor properties raise the possibility that any undesirable effects of smoking could be effected through its activity. Even though the plasma levels of vasopressin probably are not sufficient significantly to restrict coronary blood flow per se, the lack of increased flow despite increments of rate and pressure may represent a restrictive effect of low hormone concentration upon the response to these stimuli of coronary vasodilatation.

It would appear that an enhanced ratio of left ventricular work to oxygen uptake may be maintained for some time without cardiac dysfunction. Such is the case in animals with chronic complete heart block or in those subjected to expansion of intravascular volume. Such disproportion in coronary subjects, however, if large enough, could presumably produce ischemia symptoms. This circumstance, as suggested by this study, would appear to be an uncommon occurrence.

**Summary**

The myocardial and peripheral hemodynamic effects of cigarette smoking have been assessed during a steady state situation in a group of normal subjects, and compared with a group of patients with coronary artery disease.

During smoking, in both groups there was augmentation of heart rate, systemic arterial pressure, and left ventricular work, this response being somewhat greater in the coronary patients. Despite these hemodynamic alterations, neither group had a significant change in coronary blood flow, so that myocardial oxygen usage remained virtually identical with the value before smoking. There was no evidence of myocardial ischemia in the coronary subjects during smoking. The various factors, potentially responsible for the lack of myocardial blood flow increment are considered.

**Acknowledgment**

We wish to express our appreciation for the technical assistance of Miss Margaret Reese and Miss Patricia Carpenter.

**References**


11. Gorlin, R., Brachfield, N., MacLeod, C., and Bopp, P.: Effect of nitroglycerin on the coro-
Murmurs are not, as is often supposed, louder, *caeteris paribus*, in proportion as the valvular contraction is greater. On the contrary, the loudest murmurs are produced by a moderate contraction, and they become weak when it is extreme. A contraction of the mitral or tricuspid valve to only two, three, or four lines (one line = 1/12 inch) in diameter, I have frequently known to occasion little or no murmur.—J. Hope. *A Treatise on the Diseases of the Heart and Great Vessels*. London, Kidd, 1832.
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Circulation. 1961;23:365-369
doi: 10.1161/01.CIR.23.3.365

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