Effect of Aspirin on Coronary Collateral Blood Flow

John D. Altman, MD; Daniel Dulas, MD; Todd Pavek, BA; and Robert J. Bache, MD

Background. Although aspirin exerts beneficial antiplatelet activity in patients with coronary artery disease, cyclooxygenase blockade produced by aspirin causes a potentially deleterious effect by interrupting endothelial production of prostacyclin. Collateral vessels that develop in response to coronary occlusion display prominent endothelial cell proliferation and undergo vasoconstriction in response to indomethacin. This study was performed to test the hypothesis that cyclooxygenase blockade with aspirin would cause constriction of coronary collateral vessels and that such vasoconstriction would be reversed with nitroglycerin.

Methods and Results. Collateral vessel growth was induced by embolic occlusion of the left anterior descending coronary artery in dogs. Four to 6 months later, coronary collateral flow was measured as retrograde flow from the cannulated collateral-dependent artery. Aspirin (1 mg/kg i.v.) caused 70±8% blockade of the increase in coronary blood flow produced by intra-arterial arachidonic acid and decreased retrograde flow from 37±7 to 28±7 ml/min (p<0.03). Increasing the dose of aspirin to 15 mg/kg i.v. caused 91±3% blockade of the response to arachidonic acid and further decreased retrograde flow to 21±4 ml/min (p<0.01). After aspirin administration, nitroglycerin (150 µg/min i.c.) reversed the collateral constriction and increased retrograde flow to 37±10 ml/min (p<0.01).

Conclusions. These data suggest that products of cyclooxygenase metabolism cause tonic vasodilation of well-developed coronary collateral vessels. Blockade of cyclooxygenase with even low-dose aspirin caused collateral vessel constriction with a decrease in collateral blood flow. However, nitroglycerin was able to fully reverse aspirin-induced collateral vasoconstriction and restore flow to the control level. (Circulation 1993;87:583–589)

KEY WORDS • aspirin • blood flow, collateral • cyclooxygenase

Aspirin is a mainstay in the treatment of patients with acute coronary syndromes. Although aspirin exerts important antiplatelet antiaggregatory effects, aspirin could cause an unfavorable effect because the cyclooxygenase blockade that it produces suppresses endothelial production of prostacyclin. Prostacyclin exerts antiaggregatory effects on platelets and has vasodilator activity. Although coronary vessels are responsive to the vasodilator properties of prostacyclin, most physiological studies have found little evidence that endogenous prostaglandins are important in regulation of the coronary circulation in the normal intact organism.

Collateral vessels that develop in response to chronic coronary occlusion differ from normal arterial vessels in that they demonstrate marked endothelial cell proliferation and subintimal hyperplasia. We recently observed that cyclooxygenase blockade with indomethacin caused a significant decrease in collateral blood flow in a canine model of coronary artery occlusion. This finding suggested that the endothelial hyperplasia in the collateral vessels may be associated with increased production of vasodilator prostaglandins. However, indomethacin has been demonstrated to exert vasoconstrictor activity independent of its effect on cyclooxygenase. Because of the widespread use of aspirin in patients with occlusive coronary artery disease, it seemed important to determine whether this agent would also impair coronary collateral blood flow. Consequently, the present study was carried out to examine the effect of aspirin on coronary collateral blood flow.

Methods

Studies were performed in 13 adult mongrel dogs of either sex that weighed 22–28 kg and were obtained from a licensed dealer. None of these animals were used in our previous study of the effects of indomethacin on coronary collateral blood flow. Group 1 consisted of six animals that were used to determine the degree of cyclooxygenase blockade by measuring the response of coronary blood flow to intra-arterial arachidonic acid before and after administration of aspirin. Group 2 consisted of seven animals with chronic coronary artery occlusion that were used to examine the effect of aspirin on coronary collateral blood flow. All studies were performed in accordance with the “Position of the American Heart Association on Research Animal Use” adopted November 11, 1984, and under the supervision...
of the Animal Care Committee of the University of Minnesota.

**Group 1**

Six adult mongrel dogs were anesthetized with sodium pentobarbital (30–35 mg/kg i.v.), intubated, and ventilated with a Harvard respirator. A left thoracotomy was performed in the fifth intercostal space under sterile conditions. A heparin-filled PVC catheter (3.0 mm o.d.) was introduced into the ascending aorta via the left internal thoracic artery. The pericardium was opened, and a similar catheter was introduced into the left ventricle at the apical dimple. The proximal left circumflex coronary artery was dissected free, and a 5-MHz Doppler flow probe was fitted around the artery. A heparin-filled Silastic catheter (0.3 mm i.d.) was introduced into the circumflex artery distal to the flowmeter probe. The pericardium was loosely closed, and the flowmeter leads and catheters were tunneled subcutaneously to exit at the base of the neck. The chest was closed in layers. The flowmeter leads and catheters were protected by a nylon vest that the animals had been trained to wear. Catheters were flushed with heparin-saline daily to maintain patency.

Studies were performed 5–7 days after surgery. Left ventricular and aortic pressures were measured with Statham P23XL pressure transducers. Coronary blood flow was measured with a Doppler flowmeter (Craig Hartley, Houston, Tex.). Data were recorded on an eight-channel recorder (Coulbourn Instruments, Lehigh Valley, Pa.). The responses of coronary blood flow to injections of arachidonic acid or vehicle into the coronary artery catheter were observed. Arachidonic acid was dissolved in 10% ethanol in 100 mM Na₂CO₃ under nitrogen, diluted with isotonic saline to a final concentration of 1 mg/ml, and used within 1 hour after preparation. The increase in coronary blood flow produced by intracoronary arachidonic acid or vehicle (0.7 ml) was recorded in triplicate at 5-minute intervals. Aspirin (1 mg/kg) was then administered as an intravenous bolus. Thirty minutes after administration of aspirin, the responses to intracoronary arachidonic acid and vehicle were again observed. A second and a third dose of aspirin (4 and 10 mg/kg) were administered similarly. Thirty minutes after each aspirin dose, hemodynamic and coronary flow responses to arachidonic acid and vehicle were again observed. The response to vehicle was subtracted from the response to arachidonic acid, and the excess flow produced by arachidonic acid was compared with the corresponding measurement obtained after each dose of aspirin.

**Group 2**

**Induction of collateral vessel growth.** Collateral growth was induced in seven adult mongrel dogs by embolization of the left anterior descending coronary artery with a hollow plug. Animals were anesthetized with sodium pentobarbital (25–30 mg/kg i.v.), intubated, and ventilated with a respirator. The right carotid artery was isolated under sterile conditions. After administration of heparin sodium (6,000 units i.v.), an 8F Judkins right coronary artery catheter was introduced into the left coronary ostium and directed toward the anterior descending artery. A 0.014-in. angioplasty guidewire was advanced through the catheter and into the distal anterior descending coronary artery. Nitroglycerin (100 μg) was administered into the catheter to produce coronary artery dilation. The coronary catheter was then removed leaving the guidewire in place, and a hollow stainless-steel plug (2.3–2.7 mm o.d., 1.1 mm i.d., 4 mm length) was advanced along the guidewire until the plug was firmly wedged in the coronary artery. The guidewire was then removed. The position and patency of the plug were confirmed by fluoroscopy during intracoronary injection of 5 ml of 60% diatrizoate meglumine.

**Surgical preparation.** After allowing 4–6 months for collateral vessel development, animals were returned to the laboratory, premedicated with morphine sulfate (1 mg/kg s.c.), anesthetized with α-chloralose (100 mg/kg i.v. followed by 10 mg/kg per hour), intubated, and ventilated with a respirator using supplemental oxygen to maintain arterial Po₂ within the physiological range. Two 7F National Institutes of Health catheters were introduced into the femoral arteries and advanced into the ascending aorta for blood sampling and pressure measurement. A similar catheter was introduced into the left carotid artery and advanced into the left ventricle for pressure measurement. A left thoracotomy was performed in the fifth intercostal space. A pneumatic cuff occluder was fitted around the descending thoracic aorta to allow control of proximal arterial pressure. The heart was suspended in a pericardial cradle, and a PVC catheter (3.0 mm o.d.) was introduced into the left atrium. The coronary artery plug was located by palpation, and the anterior descending artery was mobilized for 1.0–1.5 cm proximal and distal to the plug. Anticoagulation was obtained with sodium heparin (200 units/kg i.v. followed by 1,000 units/hr). The artery was occluded proximally, the occluding plug was extracted, and the artery cannulated with a thin-wall stainless-steel cannula (4 mm o.d.). Coronary cannula resistance determined from the pressure decrease produced by passing measured flows of blood through the cannula was 0.097 mm Hg/ml per minute of flow. Coronary pressure was measured with a 23-gauge tube incorporated into the wall of the cannula. The proximal occlusion was removed, and a heparin-filled PE 90 tubing was introduced into the artery and advanced retrograde to the left main coronary artery to allow nitroglycerin infusion.

**Experimental protocol.** Left ventricular, aortic, and coronary pressures were measured with Statham P23XL pressure transducers. Left ventricular pressure was recorded at normal and high gain for measurement of end-diastolic pressure. Left ventricular dP/dt was obtained by electronic differentiation of the pressure signal. Data were recorded on an eight-channel direct writing recorder (Coulbourn Instruments). Measurements of intra-arterial collateral blood flow were performed by collecting retrograde flow from the coronary cannula into a graduated cylinder for 30 seconds while the cannula tip was maintained at the level of the heart. Control measurements were repeated until consistent collections were obtained; thereafter, measurements were performed in triplicate and the results were averaged. Distal coronary pressure measurements were obtained with the cannula tubing clamped. After obtaining control measurements, nitroglycerin in a dosage of 150 μg per minute was infused into the left main coronary artery. Three minutes after beginning the
infusion, hemodynamic measurements were made, and retrograde flow collections were performed. After retrograde flows returned to baseline, aspirin was administered as an intravenous bolus dose of 1 mg/kg. Hemodynamic measurements were recorded continuously, and retrograde flow measurements were obtained 30 minutes after aspirin. A second bolus dose of aspirin (14 mg/kg) was then administered intravenously. Thirty minutes after the second dose of aspirin, hemodynamic measurements were recorded, and retrograde flow collections were repeated. After completion of these measurements, intracoronary infusion of nitroglycerin and retrograde flow collection were repeated as described above.

**Statistical Analysis**

Heart rate and pressures were measured from strip-chart recordings. For animals in group 1, coronary blood flows were computed from the Doppler shift, assuming arterial wall thickness equal to 10% of the flow probe diameter, as described by Ishida et al. Hemodynamic data were analyzed using ANOVA for repeated measures. Collateral resistance was calculated by subtracting the coronary cannula pressure, during retrograde flow collection, from the mean aortic pressure and dividing by total retrograde blood flow. A value of $p<0.05$ was required for statistical significance. When a significant difference was found, the Wilcoxon signed-rank test and Student's paired $t$ test were used to examine differences between individual interventions. Data are expressed as mean±SEM.

**Results**

**Group 1**

The response to intracoronary bolus injection of arachidonic acid is shown in Table 1. Heart rate, left ventricular dP/dt, and mean aortic pressure were not altered by arachidonic acid. Intracoronary arachidonic acid caused a 102±12% peak increase in coronary blood flow and an increase in total integrated excess flow of 31±8 ml. The coronary vasodilation produced by arachidonic acid was brief in duration, with flow returning to the control level within 1 minute. Aspirin (1, 5, and 15 mg/kg cumulative dose) did not affect baseline hemodynamic measurements but produced 70±8% ($p<0.01$), 88±4% ($p=0.03$), and 91±3% ($p<0.01$) inhibitions of the coronary vasodilation produced by arachidonic acid, respectively (Figure 1).

**Group 2**

**Hemodynamic data.** Hemodynamic measurements during control conditions and following each dose of aspirin are shown in Table 2. Heart rate, left ventricular dP/dt, and left ventricular end-diastolic pressure were not affected by aspirin. Mean aortic pressure tended to increase and distal coronary pressure tended to decrease following aspirin administration, but these changes did not reach statistical significance. However, the tendency for distal coronary pressure to decrease in conjunction with a trend toward increased aortic pressure resulted in 12±5% ($p<0.05$) and 50±18%
gradient after low-dose and high-dose aspirin, respectively.

Retrograde blood flow and cyclooxygenase blockade. Retrograde flow measurements from the cannulated left descending coronary artery are shown in Figure 2 and Table 3. During control conditions, retrograde flow ranged from 15 to 68 ml/min (average, 37±7 ml/min). Thirty minutes after low-dose aspirin (1 mg/kg i.v.), retrograde flows were decreased in every animal (mean decrease, 24±5%, p<0.03). The tendency for increased aortic pressure in conjunction with the decreased retrograde flow following low-dose aspirin resulted in a 50±15% (p<0.03) mean increase in collateral vascular resistance. Following these measurements, aspirin (15 mg/kg i.v. cumulative dose) was administered. Retrograde flows were further decreased (mean decrease, 43±10%; p<0.02) and resistance was further increased (mean increase, 100±44%, p<0.02) after high-dose aspirin.

Retrograde blood flow and nitroglycerin. To assess the reversibility of aspirin-induced collateral constriction, nitroglycerin was infused before and after aspirin administration in five animals. Hemodynamic measurements and retrograde blood flows during baseline conditions and during each nitroglycerin infusion are shown in Figure 3 and Table 4. Before aspirin, baseline retrograde flows ranged from 15 to 54 ml/min (average, 30±8 ml/min). Nitroglycerin tended to increase heart rate and decrease mean aortic pressure. Before cyclooxygenase blockade, nitroglycerin caused a significant decrease in collateral resistance and an increase of retrograde blood flow (mean increase, 23±7%, p<0.01). Thirty minutes after high-dose aspirin administration, retrograde flows were decreased to 18±6 ml/min (range, 7-42 ml/min, p<0.01). At this time, nitroglycerin infusion was repeated, and retrograde flows increased by 106±35% (p<0.02). After cyclooxygenase blockade, the relative increase in retrograde blood flow produced by nitroglycerin was greater than that observed before aspirin. The greater relative increase in blood flow was the result of lower baseline retrograde flow following aspirin, whereas absolute retrograde flow rates following nitroglycerin were not different before and after aspirin administration.

Discussion

Three new findings are reported in this study. First, in this model of chronic coronary occlusion, cyclooxygenase blockade with aspirin caused a dramatic decrease of coronary collateral blood flow. Second, in contrast to several earlier studies, even low-dose aspirin inhibited endothelial prostaglandin production, and this was found to decrease coronary collateral blood flow.13,14 Finally, the aspirin-induced decrease in collateral blood flow was completely reversed by nitroglycerin. These new findings, as well as the method for determination of collateral blood flow, are discussed in detail.

Critique of Method

Retrograde flow collection from the cannulated collateral-dependent coronary artery commonly has been used to estimate collateral blood flow. This technique slightly underestimates collateral flow because not all blood is diverted retrograde into the collecting cylinder when the cannula is opened to atmospheric pressure. That is, in the well-collateralized heart, opening the coronary cannula decreases but does not abolish blood flow into the collateral-dependent region. Downey et al16 provided evidence that continuing tissue flow in the collateral region during retrograde collection is derived from microvascular communications that enter the recipient artery at a site distal to significant resistance, so antegrade flow encounters less resistance than flow back into the arterial cannula. From determinations of mean stem pressures at the origin of the collateral vessels, Harrison et al17 concluded that microvascular communications could contribute no more than 25% of total collateral blood flow. This is in agreement with studies.

---

**TABLE 2. Hemodynamic Data for Seven Dogs With Chronic Coronary Artery Occlusion (Group 2) During Control Conditions and After Administration of Aspirin in Doses of 1 and 15 mg/kg**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Heart rate (bpm)</th>
<th>Mean aortic pressure (mm Hg)</th>
<th>Distal coronary pressure (mm Hg)</th>
<th>Aortic-coronary pressure gradient (mm Hg)</th>
<th>Left ventricular dp/dt (mm Hg/sec)</th>
<th>Left ventricular end-diastolic pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>131±14</td>
<td>97±8</td>
<td>71±11</td>
<td>26±4</td>
<td>3,200±700</td>
<td>6±1</td>
</tr>
<tr>
<td>Aspirin (1 mg/kg)</td>
<td>132±16</td>
<td>107±8</td>
<td>78±9</td>
<td>29±3*</td>
<td>3,000±800</td>
<td>7±1</td>
</tr>
<tr>
<td>Aspirin (15 mg/kg)</td>
<td>121±11</td>
<td>103±8</td>
<td>64±6</td>
<td>39±5*</td>
<td>2,900±700</td>
<td>7±1</td>
</tr>
</tbody>
</table>

*p<0.05.
TABLE 3. Aortic Pressure, Residual Pressure at the Cannula Tip During Retrograde Flow Collection, Net Coronary Driving Pressure, Retrograde Flow, and Computed Collateral Vascular Resistance for Seven Dogs With Chronic Coronary Artery Occlusion (Group 2) During Control Conditions and Following Administration of Aspirin in Doses of 1 and 15 mg/kg

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mean aortic pressure (mm Hg)</th>
<th>Cannula open pressure (mm Hg)</th>
<th>Net driving pressure (mm Hg)</th>
<th>Collateral retrograde flow (ml/min)</th>
<th>Collateral resistance (mm Hg/ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>97±8</td>
<td>7±3</td>
<td>90±8</td>
<td>37±7</td>
<td>2.4±0.5</td>
</tr>
<tr>
<td>Aspirin (1 mg/kg)</td>
<td>107±8</td>
<td>6±3</td>
<td>101±7</td>
<td>28±7*</td>
<td>3.6±0.8*</td>
</tr>
<tr>
<td>Aspirin (15 mg/kg)</td>
<td>103±8</td>
<td>3±2</td>
<td>100±8</td>
<td>21±4*</td>
<td>4.8±1.3*</td>
</tr>
</tbody>
</table>

*p<0.05 vs. control.

Effect of Aspirin on Collateral Blood Flow

We recently observed that indomethacin caused a significant decrease in coronary collateral blood flow in dogs with chronic coronary artery occlusion. This was an unexpected finding since cyclooxygenase blockade with indomethacin has generally been reported to have little effect on the normal coronary circulation. Thus, we previously found that indomethacin did not alter the basal rate of coronary blood flow, reactive hyperemia, or the increase in coronary flow that occurred during treadmill exercise. Because the indomethacin-induced collateral vasoconstriction was unanticipated, it seemed important to determine whether this effect would occur with a different cyclooxygenase blocker, especially since indomethacin has been reported to exert vasoconstrictor activity independent of cyclooxygenase blockade.

Thus, Forman and associates found that indomethacin caused vasoconstriction in the atherosclerotic human coronary circulation, but pretreatment with aspirin (2,600 mg p.o.), which clearly would result in cyclooxygenase blockade, did not blunt the indomethacin-induced coronary vasoconstriction. The investigators concluded that in the atherosclerotic coronary circulation, a portion of the coronary vasoconstriction caused by indomethacin must be attributed to a mechanism other than cyclooxygenase blockade. In contrast to these findings in the atherosclerotic coronary circulation, in the present study aspirin caused a decrease in collateral flow comparable to that produced by indomethacin. These findings support the concept that it is the cyclooxygenase blockade that decreased collateral flow rather than an effect unique to indomethacin.

Effect of Aspirin on Epicardial Arteries

Because the resistance to collateral blood flow includes not only the collateral vessels themselves but also the epicardial arteries proximal to the origin of the collateral vessels, coronary artery constriction could have contributed to the observed decrease in collateral flow in response to aspirin. To determine whether cyclooxygenase blockade causes significant vasoconstriction of proximal coronary arteries, Lane and Bove used quantitative angiography to assess coronary artery cross-sectional area in anesthetized closed-chest dogs. These investigators found that cyclooxygenase blockade with indomethacin (5 mg/kg i.v.) caused no change in the cross-sectional area of epicardial coronary artery segments. These previous findings suggest that the decreased collateral flow observed in the present study was not the result of aspirin-induced vasoconstriction of coronary artery segments proximal to the collateral vessels.

Effect of Aspirin on Normal Zone Flow

Collateral flow can also be influenced by changes in normal zone blood flow. Thus, agents that produce vasodilation of coronary resistance vessels with increased blood flow to normal myocardial regions cause an increase in the pressure drop across the proximal coronary artery segment, thereby decreasing the pressure available at the origin of the collateral vessels (coronary steal). Previous studies in anesthetized animals have demonstrated that cyclooxygenase inhibitors, including aspirin, cause either no effect or slight vasoconstriction of normal coronary resistance ves-
These previous findings indicate that aspirin would not have caused changes in either the proximal coronary arteries or the coronary resistance vessels, which would cause a decrease in collateral blood flow.

**Mechanism of Action of Aspirin on Collateral Vessels**

Collateral vasocostriction produced by aspirin is analogous to the vasoconstrictor activity of cyclooxygenase blockade on the ductus arteriosus and probably is mediated through inhibition of local prostanoid production. Vascular prostaglandin production is concentrated in endothelial cells where the principal enzymatically derived metabolite of arachidonic acid is prostacyclin. Prostacyclin has been shown to cause vasodilation of coronary collateral vessels, so inhibition of endogenous prostacyclin production could explain the present findings. Alternatively, collateral vasocostriction could have occurred as blockade of cyclooxygenase caused arachidonic acid to be diverted from prostaglandin synthesis into the lipoxygenase pathway. Arachidonic acid is metabolized by lipoxygenase to form leukotrienes C4 and D4, both of which are potent vasoconstrictors. Leukotriene production occurs principally in leukocytes but has been detected in isolated canine and human coronary artery segments. However, several observations suggest that increased leukotriene production was not responsible for collateral constriction in response to aspirin in the present study. First, Lane and Bove found that cyclooxygenase blockade with indomethacin did not cause coronary artery constriction, suggesting little activity of the leukotriene pathway in coronary arterial vessels. Second, although coronary collateral vessels show perivascular inflammation early during their development, which might enhance leukotriene production, Schaper and associates found that leukocyte infiltration disappears within 8 weeks after coronary occlusion. Because the present study was performed 4–6 months after coronary occlusion, leukocyte infiltration and any tendency for increased leukotriene production would have subsided by the time the study was performed. Finally, tolerance to the vasoconstricting effect of intracoronary leukotrienes has been reported to develop within 2–4 minutes, whereas the collateral constriction in response to aspirin was stable during the 1-hour observation period. These considerations suggest that collateral vasocostriction produced by aspirin did not result from increased arachidonic acid shunting into the leukotriene pathway and more likely occurred as the result of interruption of endothelial prostacyclin production by the collateral vessels. Nevertheless, without measurements of prostacyclin levels, it is not possible to resolve the mechanism for aspirin-induced collateral constriction.

Early studies suggested that low-dose aspirin (1–5 mg/kg) might provide a cardioprotective platelet antiaggregatory effect without interfering with vascular prostaglandin production. However, subsequent studies failed to document a dose of aspirin that exerted significant antiplatelet activity without inhibiting endothelial prostacyclin production. Similarly, in the present study, aspirin in a dose of 1 mg/kg caused 70% inhibition of the coronary vasodilation produced by intra-arterial administration of arachidonic acid and decreased collateral blood flow by 24±5% (p<0.03). These findings support the concept that dosages of aspirin commonly used for antiplatelet therapy cause significant impairment of vascular prostaglandin production. The duration of this impairment was not determined in the present study.

**Clinical Implications**

Numerous studies have reported the benefit of antiplatelet therapy in preventing myocardial infarction and reducing cardiovascular mortality in patients with a previous myocardial infarction. Despite beneficial antiplatelet effects, the present findings suggest that interruption of endothelial cyclooxygenase metabolism by aspirin has potential for adversely affecting blood flow to collateral-dependent regions of myocardium. In a study of 33 men with angiographically documented clinically stable exertional angina pectoris, Steele et al examined the effects of aspirin, dipyridamole, and a combination of the two on exercise tolerance. The duration of angina-limited treadmill exercise was increased in only those individuals receiving dipyridamole alone, suggesting that any beneficial antiplatelet effect of aspirin may have been counteracted by a deleterious effect on blood flow to potentially ischemic myocardium. In patients with atherosclerotic disease undergoing diagnostic cardiac catheterization, indomethacin was reported to decrease coronary sinus blood flow and increase myocardial oxygen extraction. The reduction of coronary blood flow in response to cyclooxygen-
ase blockade in patients with coronary artery disease could have resulted from either enhanced production of vasodilator prostaglandins in the diseased vessels or myocardial dependence on collateral blood flow. Unfortunately, neither study documented the extent of collateral-dependent myocardium in their subjects.

An important finding in the present study was that collateral vasoconstriction produced by aspirin could be fully reversed by nitroglycerin. Thus, if cyclooxygenase blockade did cause myocardial ischemia because of a decrease in collateral blood flow, the present data suggest that this effect could be reversed by administration of nitroglycerin. Clearly, however, these laboratory findings must be extrapolated with care to the clinical setting.

Summary

Cyclooxygenase blockade with aspirin resulted in a substantial decrease in blood flow through well-developed coronary collateral vessels. This suggests that the endothelial cell hyperplasia observed in well-developed coronary collateral vessels is associated with increased endothelial production of vasodilator prostaglandins. Vascular prostaglandin production and collateral blood flow were impaired even with aspirin doses as low as 1 mg/kg. Importantly, however, collateral vasoconstriction produced by aspirin could be completely reversed with nitroglycerin.

References

Effect of aspirin on coronary collateral blood flow.
J D Altman, D Dulas, T Pavek and R J Bache

Circulation, 1993;87:583-589
doi: 10.1161/01.CIR.87.2.583

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1993 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/87/2/583

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/