Lignocaine in experimental myocardial infarction: failure to prevent neutrophil accumulation and ventricular fibrillation and to reduce infarct size

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ABSTRACT Growing evidence supports the concept that neutrophils accumulating in reperfused ischaemic myocardium play a detrimental role in evolving infarction. Lignocaine, an antiarrhythmic drug commonly used clinically, interferes with neutrophil function in vitro and potentially in vivo. To test the hypothesis that lignocaine may influence infarct size by reducing neutrophil accumulation in reperfused ischaemic myocardium, 31 dogs underwent a 2 h occlusion of the left anterior descending coronary artery, followed by 6 h of reperfusion. One group of dogs received saline (controls) the other a perfusion of lignocaine 0.06 mg·kg⁻¹·min⁻¹ starting 30 min before coronary occlusion and lasting for the duration of the experiment. Blood lignocaine concentrations at the onset of reperfusion were 3.3(0.6) µg·ml⁻¹. Indium labelled autologous neutrophils were injected at the time of occlusion and their accumulation in the myocardium measured by digital scintigraphy of heart slices. The area at risk and infarct size were evaluated by planimetry of the heart slices (7 mm) after perfusion of Evans blue dye and triphenyltetrazolium staining. Ventricular fibrillation occurred in six controls and in five dogs receiving lignocaine. The phenomenon occurred early during the occlusion period in the lignocaine group (five dogs) and at reperfusion in controls (five dogs; p<0.05). In the remaining 20 dogs, 10 in each group, a linear correlation was found between myocardial Indium labelled neutrophil and circulating neutrophil counts at the onset of reperfusion (r=0.076, p<0.05) and with infarct size (r=0.96 and 0.74, p<0.05). The myocardial Indium neutrophil counts per cm² of tissue were statistically similar in controls (9725(1669)) and lignocaine treated dogs (11631(3317)). Infarct size expressed as a percentage of the area at risk was also similar in both groups (controls 36.1(7.1)%; lignocaine 35.8(6.3)%).

Thus lignocaine does not reduce infarct size and myocardial neutrophil accumulation after a 2 h coronary occlusion in the dog. Furthermore, these results suggest that lignocaine may induce ventricular fibrillation during coronary occlusion.

The pathophysiological role of neutrophils in evolving myocardial infarction has been re-emphasised in recent years in models with early reperfusion.¹ ² The massive³ and rapid⁴ neutrophil accumulation reported in the reperfused ischaemic myocardium may be detrimental to normal and jeopardised, but still viable, myocytes and alter the benefits of reperfusion. Neutrophils may participate in the "no reflow" phenomenon⁵ in addition to releasing cytotoxic materials such as free radicals,⁶ ⁷ proteolytic enzymes,⁸ and active metabolites of arachidonic acid.⁹ So far, successful limitation of infarct size has been reported with leucopenic¹⁰ ¹¹ and anticomplementary agents¹² and with ibuprofen¹³ and prostacyclin,¹⁴ both interfering with leucocyte accumulation and activation in the ischaemic myocardium.

Lignocaine, an antiarrhythmic drug¹⁵ commonly
used in the coronary care unit, may apparently interfere with neutrophil mobility and mobilisation to inflammatory sites and reduce their production of free radicals. The hypothesis that lignocaine may alter neutrophil function and limit experimental myocardial infarction would be of considerable interest in the clinical setting. We reported previously that neither lignocaine nor leucopenia had a significant effect on infarct size in the dog with a 3 h coronary occlusion, a model producing infarcts of similar size to that of a permanent coronary occlusion. In the present study using the same scintigraphic evaluation approach of myocardial accumulation of autologous 111In-labelled neutrophils, we tested the hypothesis that lignocaine may reduce infarct size by reducing neutrophil accumulation after a brief coronary occlusion (2 h) followed by reperfusion, a model producing smaller infarcts (de Lorgeril, unpublished data).

Methods

ISCHAEMIA AND REPERFUSION

Mongrel dogs of either sex weighing 15-31 kg were anaesthetised with sodium pentobarbital (30 mg·kg⁻¹ iv), intubated, and ventilated with room air. The electrocardiogram lead II was monitored throughout the experiment. After an injection of pancuronium bromide (0.1 mg·kg⁻¹ iv), a left thoracotomy was performed at the fifth intercostal space. A catheter was inserted into the left ventricle through the left atrium and the pressure monitored continuously. Another catheter positioned in the right femoral vein was used for infusion and blood sampling.

The left anterior descending coronary artery (LAD) was isolated distally to the first diagonal branch and flow was measured with an electromagnetic flow probe. An adjustable micrometric occluder (Cardio-Stat, I Laval, Quebec) was used to occlude the LAD for 120 min in both control and lignocaine treated animals. Dogs that developed ventricular fibrillation twice with Hank’s balanced solution, and the cells suspended in 16 ml of bovine albumin. The cell mixture was deposited on layered double Percoll (Pharmacia) gradients of 1.072 and 1.087 g·ml⁻¹. After 30 min centrifugation (900 g), the neutrophils were collected at the interface of the gradients, washed twice with Hank’s solution, and incubated for 1 min at 37°C with 500 μCi (20 MBq) 111In-oxine (Amersham). Platelet poor plasma prepared from the heparinised blood sample was added to bind free 111In-oxine and eliminated by centrifugation. The autologous labelled neutrophils were resuspended in 5 ml of platelet poor plasma and injected intravenously at the time of the coronary occlusion. Trypan blue viability and Nitroblue tetrazolium reduction function tests were carried out on the labelled neutrophils and the results for each dog compared with those obtained with corresponding neutrophils in native whole blood. Values obtained with the labelled preparation normally fall within 5% of the reference values or the preparation is discarded.

At the end of the reperfusion period, heparin (10 000 U) was injected intravenously and the animals killed. The heart was rapidly excised and infarct size quantified as previously described. Cannulation of the LAD at the site of occlusion and of the aorta, above the coronary ostia, was followed by perfusion at both regions with cold saline (0.9%) for 5 min and subsequently by perfusion of the aorta by Evans blue dye and the LAD with saline (0.9%) at a constant pressure of 100 mmHg for 5 min. The left heart was then embedded in a polyurethane foam (MIA Chemicals, Montreal) and cut with a commercial meat slicer in 7 mm thick transverse slices. The slices were immersed in triphenyltetrazolium (TPT) 1.5% in Tris buffer (2.4%, pH 7.8) for 10 min at 37°C. The normally perfused myocardium (Evans blue positive), the area at risk (AR) of ischaemia (Evans blue negative and TPT negative) were measured by planimetry for each slice. The area at risk was expressed as a percentage of the left ventricle and the infarct size related to both the left ventricle and the area at risk.

ISOLATION AND 111IN LABELLING OF NEUTROPHILS

After anaesthesia, neutrophils were isolated and labelled with 111In according to a procedure recently described. Briefly, two samples of blood (42.5 and 20 ml) were drawn from the femoral vein into 7.5 ml of acid-citrate-dextrose and 400 U of heparin respectively. The citrated blood was allowed to sediment for 30 min after addition of 32 ml of 4% dextran 250. The leucocyte rich plasma was washed twice with Hank’s balanced solution and the cells suspended in 16 ml of dextran 40 (2.4%) containing 2% bovine albumin. The cell mixture was deposited on layered double Percoll (Pharmacia) gradients of 1.072 and 1.087 g·ml⁻¹. After 30 min centrifugation (900 g), the neutrophils were collected at the interface of the gradients, washed twice with Hank’s solution, and incubated for 1 min at 37°C with 500 μCi (20 MBq) 111In-oxine. Platelet poor plasma prepared from the heparinised blood sample was added to bind free 111In-oxine and eliminated by centrifugation. The autologous labelled neutrophils were resuspended in 5 ml of platelet poor plasma and injected intravenously at the time of the coronary occlusion. Trypan blue viability and Nitroblue tetrazolium reduction function tests were carried out on the labelled neutrophils and the results for each dog compared with those obtained with corresponding neutrophils in native whole blood. Values obtained with the labelled preparation normally fall within 5% of the reference values or the preparation is discarded.
Blood was collected at different times after the injection of the $^{111}$In labelled neutrophils for the study of their kinetics in the circulation and to assess whether the ratio between the circulating and injected radioactivity was similar among dogs, a prerequisite for the quantification of neutrophils in the infarcts based on gamma spectrometry. As reported earlier, the number of circulating $^{111}$In labelled neutrophils reaches a steady state 2 h after their injection. The equation used for the determination of the circulating radioactive neutrophil pool was: circulating $^{111}$In labelled neutrophils = No of neutrophils in the standard multiplied by (BS - PS) multiplied by 75 multiplied by body weight (kg) divided by radioactivity count of the standard, where BS is the blood sample (1 ml) count, and PS (plasma sample counts) represents traces of free or protein bound $^{111}$In. The blood volume was assumed to be 75 ml·kg$^{-1}$ of body weight.

**SCINTIGRAPHY AND QUANTIFICATION OF NEUTROPHIL ACCUMULATION**

The heart slices and two reference standards, one containing $1 \times 10^{7}$ and the other $2 \times 10^{7}$ autologous $^{111}$In labelled neutrophils and dispersed in a 7 mm deep gelatin film of 9.5 cm$^2$, were placed side by side on a medium energy collimator equipped with gamma camera (Technicare model 420/550). An 8 h acquisition was done directly on a DEC gamma-11 system. After background subtraction, a region of interest comprising the zone of increased count density was delineated. Counts of all regions of interest were obtained to total the infarct radioactivity, which was expressed in terms of numbers of $^{111}$In labelled neutrophils using the reference standards and the following formula: No of $^{111}$In labelled neutrophils per tissue = total counts of tissues multiplied by No of neutrophils in the standard divided by counts of the standard.

To allow comparison of $^{111}$In labelled neutrophil accumulation between different groups, the number of labelled neutrophils in myocardial tissue was normalised by linear regression estimation using the mean number of $^{111}$In labelled neutrophils circulating at steady state, 2 h after their intravenous reinjection, because accumulation in the ischaemic myocardium is influenced by the number of $^{111}$In labelled leucocytes injected and circulating in the blood (covariate 1). These values were corrected further for infarct size (covariate 2) and the number of radiolabelled cells expressed per cm$^2$ of infarcted tissue.

**STATISTICS**

All the data are expressed as mean(SEM) for each group. Means are compared by t test analysis, and one way analysis of variance was performed on the haemodynamic and physiological data. Linear correlation analysis was performed with standard methods. For the quantification of the labelled neutrophil counts in infarcts by digitised scintigraphy, the final comparison between the group means was done with a t test on values adjusted for the two covariates (the number of $^{111}$In labelled neutrophils circulating at onset of reperfusion and the infarct size). The critical value for the t test was chosen as $t_{n_1 + n_2 - 4}$ degree of freedom to account for the two covariate adjustment. Differences were considered statistically significant with $p<0.05$. A Fisher adjusted $\chi^2$ test was used to compare between group incidence of ventricular fibrillation.

**Results**

Thirty one dogs underwent surgery and 20 (10 in each group) completed the study. Eleven animals, six controls and five receiving lignocaine, developed ventricular fibrillation and were excluded. In five of the six controls, ventricular fibrillation was observed during the first hour of reperfusion and one 5 min after occlusion, whereas all five ventricular fibrillations in the lignocaine group occurred during the first 20 min after occlusion ($p<0.02$).

The mean lignocaine serum concentration at the onset of reperfusion was 3.3(0.64) (range 1.7-6.8) ng·ml$^{-1}$, the therapeutic range in man being 1.5-5.0 ng·ml$^{-1}$. Physiological and haemodynamic data are summarised in table 1. The two groups were statistically similar for weight, packed cell volume, and platelet and leucocyte counts. Heart rate, left ventricular end diastolic pressure, pressure rate product, and LAD flow were also similar between the groups, before as well as during the experiment. Intragroup comparisons indicate that only left ventricular end diastolic pressure increased ($p<0.05$) after occlusion and remained increased after 30 min of reperfusion in both groups.

As summarised in table 2, the myocardial area at risk was statistically identical in the two groups and involved approximately one third of the left ventricle. Infarct size expressed as a percentage of the area at risk or as a percentage of the left ventricle was also similar in the lignocaine and control dogs and involved 36% of the area at risk or about 12% of the left ventricle.

**NEUTROPHIL LABELLING AND FUNCTION**

Neutrophil suspensions were platelet free and were contaminated with less than 5% by red blood cells and other leucocytes. Nitroblue tetrazolium and Trypan blue tests on labelled cell preparations varied within 5% of the corresponding values obtained with leucocytes in native blood. The mean number of
TABLE 1  Group characteristics and haemodynamic data. Values are mean(SEM)

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Lignocaine group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of dogs</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>22.4(1.6)</td>
<td>23.2(1.2)</td>
</tr>
<tr>
<td>Packed cell volume (%)</td>
<td>43.3(1.6)</td>
<td>46.6(2.2)</td>
</tr>
<tr>
<td>Haemoglobin concentration (g/dl)</td>
<td>15.1(0.6)</td>
<td>16.3(0.7)</td>
</tr>
<tr>
<td>Platelets (10^9 litre^-1)</td>
<td>296(26)</td>
<td>326(40)</td>
</tr>
<tr>
<td>Leucocytes (10^9 litre^-1)</td>
<td>8.7(1.5)</td>
<td>10.2(1.4)</td>
</tr>
<tr>
<td>Haemodynamic data:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before occlusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>163(9)</td>
<td>162(7)</td>
</tr>
<tr>
<td>LVEDP (mmHg)</td>
<td>6.1(0.6)</td>
<td>6.5(1.4)</td>
</tr>
<tr>
<td>RPP (b/min × mmHg × 10^5)</td>
<td>215(18)</td>
<td>219(18)</td>
</tr>
<tr>
<td>LAD flow (ml/min)</td>
<td>27.6(3.8)</td>
<td>24.6(3.1)</td>
</tr>
<tr>
<td>1 h occlusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>163(8)</td>
<td>161(6)</td>
</tr>
<tr>
<td>LVEDP</td>
<td>9.3(0.8)*</td>
<td>11.7(1.8)*</td>
</tr>
<tr>
<td>RPP</td>
<td>211(16)</td>
<td>204(15)</td>
</tr>
<tr>
<td>2 h occlusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>170(7)</td>
<td>157(7)</td>
</tr>
<tr>
<td>LVEDP</td>
<td>9.2(1.1)*</td>
<td>11.7(1.7)*</td>
</tr>
<tr>
<td>RPP</td>
<td>223(16)</td>
<td>208(14)</td>
</tr>
<tr>
<td>After 30 min reperfusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>168(6)</td>
<td>154(6)</td>
</tr>
<tr>
<td>LVEDP</td>
<td>8.3(1.05)*</td>
<td>8.7(1.6)</td>
</tr>
<tr>
<td>RPP</td>
<td>209(10)</td>
<td>204(15)</td>
</tr>
<tr>
<td>LAD flow</td>
<td>32(6.5)</td>
<td>25(8.1)</td>
</tr>
</tbody>
</table>

HR=heart rate (beats.min^-1); LVEDP=left ventricular end diastolic pressure (mmHg); RPP=rate-pressure product (beats.min^-1 × mmHg × 10^5); LAD=left anterior descending artery.

*p<0.05 vs before occlusion.

TABLE 2  Myocardial area at risk and infarct size. Values are mean(SEM)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Controls</th>
<th>Lignocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of dogs</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Area at risk (% of LV)</td>
<td>34.3(2.3)</td>
<td>31.7(1.6)</td>
</tr>
<tr>
<td>Infarct size:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of AR</td>
<td>36.1(7.1)</td>
<td>35.8(6.3)</td>
</tr>
<tr>
<td>% of LV</td>
<td>12.9(2.5)</td>
<td>11.7(2.2)</td>
</tr>
</tbody>
</table>

AR=area at risk; LV=left ventricle.

labelled neutrophils injected was statistically identical among groups: 123(24) × 10^6 in controls and 140(26) × 10^6 in lignocaine treated dogs. Injected radioactivity was also identical: 308(11) μCi (controls) and 305(9) μCi (lignocaine). Circulating labelled cell counts were statistically similar among groups at onset of reperfusion (controls 16.6(6) × 10^6; lignocaine 27.1(13) × 10^6) and throughout the reperfusion period. However, we observed a linear decay in the lignocaine group (5.7% per hour) that differed (p<0.05) from that of the control group (1.9% per hour).

MYOCARDIAL NEUTROPHIL ACCUMULATION

Of the 20 scintigraphic studies, all but four (one in controls and three in the lignocaine group) produced positive scintigraphic images (fig 1). The four negative scintigrams were obtained in animals who failed to develop infarction (1 case) or had very small infarcts (0.9% LV: 1 case; 4% LV: 2 cases). Interestingly, these animals showed very low circulating counts of labelled neutrophils with a...
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Finally, the myocardial neutrophil accumulation per square centimetre of necrosis was also statistically similar between the two groups (controls 9725(1669); lignocaine 11631(3317)) (fig 3).

Discussion

Previous studies of the effect of lignocaine on myocardial injury have led to controversial results. In a permanent coronary occlusion model, Boudoulas and colleagues observed a reduction of myocardial injury by lignocaine, based on evaluations by epicardial electrocardiographic mapping and creatine phosphokinase plasma concentrations. In a 3 h LAD occlusion dog model producing an infarct size similar to permanent occlusion and evaluated by tetrazolium staining, we failed to demonstrate any benefit of lignocaine. However, in other models with coronary occlusion of 1 h or less and with a somewhat similar methodology for estimation of infarct size but shorter reperfusion periods, lignocaine reduced infarct size. Considering these variations related to the models and the technology used and that lignocaine can potentially modify leucocyte function and ultimately influence infarct size, we evaluated the effect of the drug on myocardial neutrophil accumulation or on infarct size at therapeutic plasma concentrations.

Several studies describing the dramatic effects of lignocaine on neutrophil function in vitro refer to concentrations of lignocaine far above the human therapeutic range. Other studies using therapeutic concentrations failed to demonstrate any significant effect of lignocaine on neutrophil function. Whatever the above issue may be, we observed that lignocaine has no effect on neutrophil accumulation in the myocardial ischaemic tissue. However, this result does not rule out an effect of lignocaine on production and release of toxic superoxide anions, as suggested by the study of Peck and colleagues, who reported decreased oxygen free radical production by neutrophils from lignocaine treated patients. However, neutrophils from lignocaine treated patients still retained their ability to kill bacteria in vitro, a property which is linked to an effective free radical release by phagocytosing neutrophils. These results support the view that in vivo at therapeutic concentrations the effect of lignocaine is too weak to produce any significant inhibition of neutrophil function that could result ultimately in a benefit on infarct size, as observed with oxygen radical scavengers.⁷

FIG 2 Relation between myocardial $^{111}$In labelled neutrophil accumulation and infarct size in lignocaine and control animals. Neutrophil counts are normalised according to circulating $^{111}$In labelled cells at onset of reperfusion. Infarct size is expressed as the surface area (cm$^2$) of necrosis (TPT negative) on heart slices (7 mm).

FIG 3 (a) Myocardial $^{111}$In labelled neutrophil accumulation (per cm$^2$ myocardial infarct) and (b) infarct size (% of the area at risk) are statistically similar in both lignocaine and control groups.

recovery at onset of reperfusion of only 2.3%, 7.3%, and 2% of the injected radioactivity. Nevertheless, these data were included in the final analysis.

Myocardial $^{111}$In labelled neutrophil counts estimated from the sum of digitised tissue activity for each dog correlated significantly with the number of circulating labelled neutrophils at reperfusion in control ($r=0.76, p<0.01$) and lignocaine ($r=0.96, p<0.001$) groups. The two regression equations were statistically similar. Myocardial labelled cell counts normalised for each dog according to the mean circulating $^{111}$In labelled neutrophil counts at onset of reperfusion closely correlated with infarct size expressed in square centimetre of necrosis or as a percentage of the area at risk (fig 2). Correlation coefficients were respectively 0.95 and 0.80 in controls and 0.74 and 0.82 in the lignocaine group. The linear regressions between the two groups were statistically similar. Finally, the myocardial neutrophil accumulation per square centimetre of necrosis was also statistically similar between the two groups (controls 9725(1669); lignocaine 11631(3317)) (fig 3).
In the present study, we found that lignocaine may have influenced in some way the kinetics of the circulating leucocyte pool, as indicated by the more rapid decay in circulating $^{111}$In labelled neutrophils after lignocaine therapy. However, our approach cannot distinguish between an effect of the drug on mobilisation of leucocytes from the marginal pool and an increased turnover in the blood produced by leucocyte accumulation to inflammatory sites. Nevertheless, these changes had no measurable effect in our studies since the $^{111}$In labelled neutrophil circulating counts remained statistically identical in treated and untreated groups throughout the experiments.

The hypothesis that neutrophils could interfere with collateral circulation during ischaemia and ultimately influence infarct size, a reaction that could potentially be influenced by lignocaine, was not investigated in the present study. We measured the overall myocardial neutrophil accumulation taking place during both occlusion and reperfusion; it appears very unlikely that a similarity between the experimental groups in terms of leucocyte accumulation and infarct size could be due to initial group differences in collateral flow, since lignocaine, at therapeutic concentrations has no influence on myocardial regional blood flow nor on left ventricular stroke work.

The discrepancy between our results and those of Nassar and colleagues who found similar reductions of infarct size with low and high dosages of lignocaine may be explained by the very brief (40 min) period of occlusion used by these investigators that often fails to produce significant necrosis in several dog preparations. In this context, lignocaine may possibly have some protective effect unrelated to myocardial leucocyte accumulation when a large mass of the ischaemic tissue may still present reversible damage. Extending the ischaemic period beyond this step may lead to complete loss of protection by lignocaine, although reperfusion may still prevent a further increase in infarct size if established within 3 h of occlusion. These results with lignocaine contrast with the sustained protection on infarct size reported by several groups using calcium antagonists in models with prolonged or permanent coronary occlusion.

Although the specific aim of the study was not the investigation of the antiarrhythmic properties of lignocaine, we observed that ventricular fibrillation followed a different pattern in the two experimental groups. As a matter of fact, all the episodes of ventricular fibrillation in the lignocaine group occurred within the first 20 min after coronary occlusion, whereas in the control group all the episodes, with the exception of one case, occurred during the first hour of reperfusion. Although the number of cases is small, these results strongly suggest that lignocaine may have favoured the occurrence of ventricular fibrillation at the onset of coronary occlusion. Previous animal studies have failed to demonstrate consistent benefit by lignocaine pretreatment. Moreover, lignocaine may potentially aggravate arrhythmias. As the observation was made after abrupt coronary occlusions in anaesthetised open chest animals, interpretation of these data must be limited to such experimental models in which lignocaine has obviously no therapeutic value for preventing ventricular fibrillation at the onset of ischaemia. On the other hand, in our study, lignocaine may have had a protective effect on reperfusion arrhythmias. However, ventricular fibrillation associated with reperfusion has generally been correlated with the duration of myocardial ischaemia and with a history of arrhythmia during coronary occlusion. It can be argued that in our lignocaine group all the dogs at risk of developing ventricular fibrillation at reperfusion were already dead after the ischaemic period, which explains the low incidence of ventricular fibrillation during reperfusion in the lignocaine treated group. Finally, animals as well as human studies have indicated that lignocaine was ineffective in preventing either type of reperfusion ventricular tachycardia or fibrillation.

CONCLUSION

In the anaesthetised dog model submitted to a 2 h coronary occlusion followed by 6 h reperfusion lignocaine had no significant effect on myocardial neutrophil accumulation or on infarct size. In addition, lignocaine failed to prevent ischaemic ventricular fibrillation and potentially favoured their occurrence. Finally, our quantitative method of measuring total myocardial neutrophil accumulation appears to be valuable for evaluating the influence of any pharmacological intervention on myocardial neutrophil accumulation in myocardial ischaemia and reperfusion.

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References

Lignocaine in experimental myocardial infarction


Correspondence

Laser angioplasty in peripheral vascular disease

Sir,

The exciting laser angioplasty success described by Pilger and colleagues (1988;22:149-53) in “Laser angioplasty with a contact probe for the treatment of peripheral vascular disease” was dampened only by their inability to ablate heavily calcified lesions and the potential for thermal damage from the continuous wave Nd:YAG laser radiation. The authors indicate that they might prefer the high intensity, strongly absorbed, pulsed radiation from the excimer laser if a suitable optical delivery system could be developed. That is a challenging task because the high intensity of the excimer laser radiation makes it ablate optical fibres almost as readily as tissue.

Recently, a new laser has been identified that emits radiation that readily ablates calcified plaque, causes minimal thermal injury, and is easily transmitted by conventional quartz optical fibres.1-4 This is the pulsed dye laser; it emits 1-50 ms duration pulses of radiation at wavelengths ranging from 390 to 850 nm and may be frequency doubled to obtain ultraviolet radiation similar to that produced by the excimer laser. The optimum wavelength appears to be about 450-500 ms where plaque absorption is strong owing to yellow carotenoid pigments in the plaque. Although it ablates soft plaque by a thermal mechanism, it ablates calcified plaque by a plasma mediated process that is not completely understood. The plasma mediated process is very efficient and occurs with laser pulses that do not ablate normal artery. This selective ablative effect may offer an additional margin of safety to the laser angioplasty procedure.

Radiation from this pulsed dye laser can be transmitted by the fibre device used by Pilger and colleagues. We can get up to 150 mJ/pulse of 480 nm radiation at a 10 ns pulse duration through the fibre at a pulse repetition rate of 5 Hz. This will ablate soft and calcified human plaque and thrombus in vitro. Perhaps using the pulsed dye laser will help overcome the problems associated with using laser radiation to treat calcified lesions.

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References