NITROPRUSSIDE AND CYANIDE

Sir,—An otherwise excellent and thorough report by Vesey, Cole and Simpson (1976) fails to acknowledge or refute a hypothesis which has already appeared in this Journal (Smith and Kruszyna, 1976a) about the mechanism by which cyanide is released from nitroprusside in vitro, and the significance of that reaction for blood cyanide concentrations. We are delighted with the confirmation that “The red cell cyanide content (after nitroprusside) has no apparent toxicological significance.” As we have noted previously, it is biologically inactive because it is bound in the form of cyanmethaemoglobin (Smith and Kruszyna, 1974, 1976b).

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REFERENCES


Sir,—We apologize for failing to acknowledge the interesting findings of Smith and Kruszyna (1974, 1976a) in our recent communication to this Journal (Vesey, Cole and Simpson, 1976). Their work is an important contribution to our understanding of the breakdown of sodium nitroprusside (SNP) in vitro and probably explains a number of our observations. We were intending to make what we hoped would be a more intelligent comment on completion of work in vivo and in vitro, now in progress.

The fact that we found 98% of the total blood cyanide (HCN) in the erythrocytes (RBC) of patients immediately following the infusion of SNP is consistent with their conclusion that haemoglobin is involved in the breakdown of SNP (Smith and Kruszyna, 1974). Our reason for suggesting that red blood cell HCN is of no toxicological significance at the concentrations we reported was that some of these values, which were for patients suffering no toxic effects, were greater than reported whole blood HCN concentrations for persons who died from cyanide poisoning. We cannot comment yet on the form in which HCN is retained in the red cell, but on the basis of Smith and Kruszyna’s results only a fraction of this (about 20%) would be attached to the methaemoglobin produced in the reduction of SNP (Smith and Kruszyna, 1976b).

Our findings in vitro are similarly consistent with their hypothesis. Fresh human blood, incubated for 2 h at 37 °C, yielded 93% of the theoretical amount of HCN with SNP concentrations which might be expected clinically (5–25 μmol/litre; 1.5–7.5 mg/litre). Of this 93% was found in the red cells and 7% in plasma. When the same quantity of washed red cells was incubated with the same concentrations of SNP in saline about 72% of the theoretical yield of HCN was obtained after 2 h. Proportional amounts of plasma from the same blood incubated with the same concentrations of SNP, for the same period of time, produced 22% of the theoretical yield of HCN. This suggests that some of the SNP breaks down in the plasma (Vesey, Cole and Simpson, 1975) and may contribute about one-fifth of the total blood HCN. Thus, since HCN is lipid soluble and enters the cells readily, the HCN produced in the plasma may contribute to that found in the red cells rather than vice versa, as is implicit in the hypothesis of Smith and Kruszyna (1974, 1976b).

In a recent series of experiments (to be published) dogs have been given a bolus dose of SNP 1 mg/kg i.v. or an equivalent dose of KCN (1.09 mg/kg), or were infused at a steady rate over the course of 1 h with SNP 1.5 mg/kg. Measurement of blood cyanide concentrations indicates that

**Table I. Blood cyanide concentrations (mean ± SEM) in dogs receiving either potassium cyanide (KCN) or sodium nitroprusside (SNP)**

<table>
<thead>
<tr>
<th></th>
<th>Bolus KCN* (n = 6)</th>
<th>Bolus SNP* (n = 7)</th>
<th>Infused SNP† (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time to achieve peak plasma cyanide (min)</strong></td>
<td>2</td>
<td>5–10</td>
<td>45 (during infusion)</td>
</tr>
<tr>
<td>Peak plasma HCN (mean ± SEM) (μmol/litre)</td>
<td>26.4 ± 7</td>
<td>2.2 ± 0.3</td>
<td>1.39 ± 0.073</td>
</tr>
<tr>
<td>Peak plasma as % of total blood HCN</td>
<td>18</td>
<td>3.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Plasma HCN concentrations at time of peak RBC HCN (μmol/litre)</td>
<td>11.5 ± 3.1</td>
<td>1.6 ± 0.38</td>
<td>1.37 ± 0.078</td>
</tr>
<tr>
<td>Plasma HCN concentrations at time of peak RBC HCN (%)</td>
<td>8.5</td>
<td>1.7</td>
<td>1.1</td>
</tr>
<tr>
<td><strong>Time to achieve peak RBC HCN (min)</strong></td>
<td>5</td>
<td>20</td>
<td>End of infusion</td>
</tr>
<tr>
<td>Peak RBC HCN (mean ± SEM) (μmol/litre)</td>
<td>124 ± 12.5</td>
<td>95.3 ± 5</td>
<td>119 ± 9</td>
</tr>
<tr>
<td>Peak RBC HCN as % of total blood HCN</td>
<td>91.5</td>
<td>98.3</td>
<td>98.9</td>
</tr>
<tr>
<td>RBC HCN at time of peak plasma HCN (μmol/litre)</td>
<td>121.3 ± 7.3</td>
<td>67 ± 4.7</td>
<td>99 ± 9</td>
</tr>
<tr>
<td>RBC HCN at time of peak plasma HCN as % of total blood HCN</td>
<td>82</td>
<td>96.8</td>
<td>98.6</td>
</tr>
</tbody>
</table>

* Following the bolus dose blood samples were taken at 2, 5, 10, 20, 40, 80, 160 and 240 min.
† During infusion, samples were taken at intervals of 15 min and after the end of infusion, samples were taken at intervals of 10, 20, 30, 45 and 60 min.
the concentration reaches a maximum in the plasma initially and that peak red cell HCN concentrations occur at a later stage (table I). This would suggest also, as in the in vitro work, that there is a reaction between SNP and a plasma constituent followed by diffusion of some of the released HCN into the red cell whilst SNP enters the red cells slowly and generates HCN by reaction with haemoglobin. The results are not consistent with the suggestion that reaction occurs first in the red cell and then HCN diffuses into the plasma (Smith and Kruszyna, 1974, 1976b). These two processes acting together would explain the evanescent hypotensive action of SNP.

Although, in all three groups of dogs, maximum mean plasma thiocyanate concentrations were attained about 2 h after injection or infusion, there was a difference in the percentage of the KCN or SNP cyanide which was converted to thiocyanate (bolus KCN, 82%; bolus SNP, 63%; infused SNP, 64.5%). This would suggest that, for SNP, 12-14% less than the expected amount of the cyanide was available for detoxication and could be trapped as cyanomethaemoglobin as proposed by Smith and Kruszyna (1974, 1976b).

Whilst commenting on the points raised by Smith and Kruszyna (above and in 1976b), we would take this opportunity to point out that any published values for HCN concentrations in whole blood or unwashed erythrocytes, assayed by first acidifying the sample, may be subject to error, since in this process oxyhaemoglobin converts some of the SCN to HCN (Vesey and Wilson, in preparation). This fact would explain the anomalous finding that the toxicity of SCN injected into mice is unaffected by cyanide antidotes, although whole blood cyanide concentrations appear to be greater than those following a lethal dose of NaCN (Smith and Kruszyna, 1976a).

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REFERENCES


INABILITY TO REMOVE THE METAL STYLET FROM A CENTRAL VENOUS CATHETER

Sir,—An “Inside needle catheter” (C. R. Bard, Inc., Murray Hill, New Jersey) (14-gauge needle, 16-gauge catheter) central venous catheter was selected for insertion into the right internal jugular vein of a patient scheduled for radical abdominal surgery. The catheter (32.4 cm in length) contains an internal metal stylet. Using a sterile technique, the needle was disassembled and attached to a 10-ml syringe, leaving the catheter and its internal metal stylet intact. Puncture of the internal jugular vein was made without difficulty, and venous blood was aspirated freely. The syringe was removed and the catheter, with its metal stylet intact, was advanced through the needle without any resistance. When the catheter was advanced as far as the needle hub, the needle was withdrawn from the vein. Traction on the flow control plug, in order to remove the stylet, met with resistance and the stylet could not be withdrawn.

Fig. 1. Overall view of catheter.

Fig. 2. Close-up view of the knot in the distal part of the catheter.

A chest x-ray revealed the tip of the catheter lying within the superior vena cava just proximal to the right atrium. The entire catheter, stylet and needle were removed. When the catheter tip was at the level of the subcutaneous tissue, it could not be withdrawn through the skin surface. A minor skin incision, over the site of introduction of the catheter, allowed complete withdrawal of the catheter. Examination of the catheter (figs 1, 2) revealed a tight knot in the distal part with the stylet still intact.

We are aware of previous reports dealing with the hazards of central venous catheters (knotting, looping, shearing, etc.). However, we are not aware of any accounts dealing with inability to remove the metal stylet.

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