**Title:** IONIC AND NEWER NONIONIC CONTRAST MEDIA ADVERSELY AFFECT oxyhemoglobin dissociation

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**Introduction:** Oxygen delivery to tissue depends on chemical dissociation of molecular oxygen from hemoglobin in capillary blood. Previous studies have demonstrated that the ionic contrast media used traditionally in angiographic procedures may inhibit this process, thus jeopardizing oxygenation of the tissue (1,2). This undesirable effect of the ionic agents has been attributed mainly to high osmolality, but non specific chemotoxicities may also contribute (3,4). In light of the reduced osmolality and purported improved chemical properties of the newly developed nonionic contrast media, it might be expected that these agents would be relatively free of adverse effects on oxygen dissociation. The present study was undertaken to test this hypothesis by comparing red cell oxyhemoglobin dissociation (PSO) and the Bohr effect (change in log PSO/change in pH) in the presence of an ionic contrast agent (Iovue 370) to that in the presence of a nonionic contrast agent (Hypaque 76).

**Methods:** A 20 ml sample of venous blood was drawn from 8 conditioned, heartbeatsfree dogs into syringes containing sodium heparin. Aliquots of the blood samples and of each contrast agent were separately equilibrated at 37°C with each of three low oxygen gas mixtures (3.0%, 3.5%, or 4.0% O2; 5.6% CO2; balance nitrogen) in an IL 237 tonometer. The equilibrated blood samples, alone or after mixing with the equilibrated contrast agent, were analyzed immediately for PO2, PCO2, pH, and percent oxyhemoglobin saturation with an Instrumentation Laboratory 1306/482 blood gas-oximeter system. The concentration of Iovue 370 and Hypaque 76 used was 0.250, 0.125, 0.054 ml/ml whole blood. PO2 required for 50% oxyhemoglobin saturation (PSO) was calculated from a three point regression analysis of the linear portion of the oxyhemoglobin dissociation curve. The Bohr Factor (change in log PSO per change in pH) was computed and averaged for two changes in pH, 7.4 to 7.3 and 7.3 to 7.2. Statistical significance of effects of contrast agents was evaluated with a randomized block analysis of variance in conjunction with the Student-Newman-Keuls test.

**Results:** Table 1 demonstrates that the ionic and nonionic contrast media caused similar leftward shifts in the oxyhemoglobin dissociation curve (decreasing PSO) at standard pH 7.4. The blood samples had normal hematocrits and, carboxy- and methemoglobin levels. Both the ionic and nonionic media significantly reduced the Bohr Factor (BF) obtained at the two pH intervals. While these effects were evident at all concentrations of the contrast agents evaluated, they appeared most prominent at the highest concentrations (Table 1).

**Discussion:** The present findings indicate that the nonionic and ionic contrast agents caused similar derangements to oxyhemoglobin dissociation in vitro. Both agents caused leftward shifts in the oxyhemoglobin dissociation curve, i.e., decreased PSO, at standard pH 7.4 indicating increased oxygen affinity of the hemoglobin in their presence. In addition, both contrast media attenuated the rightward shift in the oxyhemoglobin dissociation curve normally seen with decreases in pH (Bohr effect). This in vitro evidence suggests that high blood concentrations of either the ionic or nonionic contrast agent may cause tissue oxygen deficits, especially under conditions of increased metabolic rate or reduced blood flow when rightward shifts of the oxyhemoglobin dissociation curve (due to reduced pH and elevated PCO2 and temperature) are an important mechanism for maintaining adequate tissue oxygenation. In conclusion, the reduced osmolality and purported superior chemical characteristics of a new nonionic contrast agent did not free this agent of the adverse effects on oxyhemoglobin dissociation.

**References:**


**Table 1.** Effect of Contrast Media (0.25 ml/ml whole blood) on red cell PSO and Bohr Factor (BF).

<table>
<thead>
<tr>
<th>pH</th>
<th>7.2</th>
<th>7.3</th>
<th>7.4</th>
<th>BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>39.3 ± 3.9</td>
<td>38.7 ± 5.6</td>
<td>30.6 ± 6.4</td>
<td>0.54 ± 0.01</td>
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<tr>
<td>Hypaque</td>
<td>31.4 ± 6.7</td>
<td>29.2 ± 6.7</td>
<td>27.2 ± 7.9</td>
<td>0.31 ± 0.02</td>
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<tr>
<td>Iovue</td>
<td>31.1 ± 6.7</td>
<td>29.7 ± 6.7</td>
<td>27.5 ± 8.8</td>
<td>0.33 ± 0.02</td>
</tr>
</tbody>
</table>

Values are mean ± S.E. in 8 dogs. *p<0.05, from each pH + PCO2.05, from baseline.

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