SHORT COMMUNICATION

The Intravenous Intralipid Tolerance Test

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The half-life of an intravenously injected bolus of intralipid 20% was measured in normal rats in order to assess its relationship to reticuloendothelial system (RES) activity. Groups of animals were studied following various treatments, and the results compared to measurement of carbon clearance in similar groups. The RES effects of silica and C parvum were confirmed by the carbon clearance test, but no effect was seen on the half-life of intralipid. Intralipid clearance was shortened by fasting and the administration of intravenous heparin, neither of which affected carbon clearance. It is concluded that the intravenous intralipid test has no place in the assessment of RES function.

Key words: intralipid, lipid, reticuloendothelial system, heparin

Intralipid is a commercial fat preparation widely used for parenteral nutrition of patients. It is a triglyceride emulsion whose particulate size is between 0.1 and 0.2 μm in diameter, and therefore is suitable for phagocytosis by the reticuloendothelial system (RES). Phagocytosis has been demonstrated by circulating human monocytes [5] and deposits recorded in the RES of patients after long-term administration [4, 6]. The half-life of injected intralipid has been used by some authors in the assessment of RES activity in both man [8] and the dog [7]. However, other authors have described a similar test to study tissue lipolysis as part of the metabolic assessment of patients [1, 9, 12] and in dogs [1]. We have therefore attempted to establish which of these routes are principally represented by the half-life of injected intralipid, using an animal model in which comparison is made to carbon clearance.

MATERIALS AND METHODS

Two hundred and twenty-gram Sprague Dawley rats were divided into test groups of around ten animals. Different groups were used for the intralipid and carbon clearance tests with each of the following manoeuvres. 1) Controls—0.1 ml saline IV; 2) heparin sodium 250 U/kg IV 10 minutes before testing; 3) fasted animals

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were caged individually and received 5 gm of feed per day (1/3 of normal intake) for 4 days before study; 4) silica (Dorentrup Quartz No. 12, a kind gift from Dr. A.C. Allison) 500 mg/kg IP 6 days prior to testing; 5) corynebacterium parvum (Wellcome Labs, Beckenham, U.K.) 7 mg/kg IV 7 days before study.

**Clearance Studies**

Under general anesthesia, intralipid 20% (Kabivitrum, Ltd.) was injected IV at a dose of 0.5 ml/kg. Blood samples in the quantity of 0.1 ml were taken from the tail vein at 2-minute intervals for 12 minutes after injection, diluted to 1 ml in normal saline, centrifuged at 3000 rpm for 5 minutes, and the turbidity of the supernatant was measured spectrophotometrically at 580 nm. Carbon clearance was measured under general anaesthesia, when a bolus of diluted Pelikan Ink (C11/1431a Gunther Wagner, 8 mg/100 gm) in 1% gelatin was given IV, and 25 µl blood samples taken at 2-minute intervals for 14 minutes. These were haemolysed in 3 ml of water and the absorbance of the supernatant measured at 650 nm. Half-lives were then calculated using a semi-log plot. Statistical comparisons were made using the Student’s t-test.

**RESULTS AND DISCUSSION**

Both clearance tests produced satisfactory and consistent results from which individual values of half-life could be accurately calculated. Table 1 summarises the effects of each manoeuvre on these. Silica is toxic to the RES [10], and C parvum causes RES hypertrophy and increased phagocytosis [15]. Carbon clearance was significantly affected by these manoeuvres, but no comparable effect was seen on the half life of intralipid. Conversely, animals which were fasted in order to stimulate gluconeogenesis showed a significant increase in lipid clearance. A striking acceleration was also seen following the IV administration of heparin. Although Saba and Antikatzides [13] have described a stimulation of RES activity by heparin, this was a marginal effect and not seen in our measurements of carbon clearance. However, marked stimulation of lipoprotein lipase activity is always seen following exposure to heparin [14], and we have no doubt that the changes observed in these experiments were produced by this mechanism.

Contrasting conclusions about the fate of various injected lipid suspensions have been described by other authors, with differences which may relate to the individual size and nature of fat particles. DiLuzio and Riggi suggested that intralipid is not principally taken up by the RES because they observed no effect of glucan on its half-

<table>
<thead>
<tr>
<th>Group</th>
<th>Carbon clearance</th>
<th>Intralipid clearance</th>
<th>No. rats</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>6.2 ± 2.4</td>
<td>8.7 ± 3.0</td>
<td>14/11</td>
</tr>
<tr>
<td>Silica</td>
<td>13.9 ± 7.3*</td>
<td>7.6 ± 1.8</td>
<td>10/11</td>
</tr>
<tr>
<td>C parvum</td>
<td>3.8 ± 0.7</td>
<td>5.7 ± 1.3</td>
<td>10/9</td>
</tr>
<tr>
<td>Heparin</td>
<td>7.6 ± 2.6</td>
<td>2.1 ± 1.0*</td>
<td>11/10</td>
</tr>
<tr>
<td>Fasting</td>
<td>5.7 ± 0.7</td>
<td>4.2 ± 1.4*</td>
<td>9/10</td>
</tr>
</tbody>
</table>

*P < 0.01 in comparison to control values.
life [3]. Rossner measured tissue uptake of intralipid during continuous intralipid infusion and found the major consumption to be by muscle and fat, with a negligible contribution from liver and spleen [11]. These observations are consistent with the recent concept that human chylomicrons are first hydrolysed by fat and muscle to form smaller “chylomicron remnants” which are then taken up by hepatic parenchymal cells [2]. While it is likely that some intralipid particles are phagocytosed by the RES following an IV bolus, we do not feel that this is its principal fate. Our studies are consistent with the concept that its half-life is primarily determined by muscle and fat lipolysis. It is clear therefore that the half-life of injected intralipid cannot be used to measure RES activity.

REFERENCES