
**Letters to the Editor**

**Ation that Dr Royall and colleagues enjoyed our paper, and we entirely accept their comments about the use of EXIT25 in various settings.**

Our purpose was to explore the possibility of using EXIT25 to identify patients who are unlikely to learn an adequate inhaler technique, hence the need to impose the concept of a threshold. As we made clear, such an approach could only ever be part of a broader assessment. Also, the study in question is one of a series to refine our understanding of this difficult area of patient management, and will, we believe, fall into perspective as we publish our further findings.

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**Amiodarone and cirrhosis**

SIR—In a recently published case report of pseudo-alcoholic hepatotoxicity secondary to amiodarone, Singhal et al. claimed that ‘severe hepatic toxicity and cirrhosis with low dose amiodarone has not been reported in the English language literature’ and mentioned it as an ‘exceedingly rare’ complication [1].

We would like to make a few comments. First and foremost, the entity of amiodarone hepatotoxicity mimicking alcoholic liver disease had been well characterised in the seminal paper almost two decades ago [2]. Thereafter, numerous cases of amiodarone-associated cirrhosis had been reported from English literature alone [3–13] although the exact incidence (obviously subject to ascertainment bias with varying liver biopsy rates) remained unknown. Similar to the case under discussion, the majority of amiodarone-associated cirrhosis complications were fatal. Among them, cumulative dose of amiodarone varied widely; in particular, several of the cases [6, 8, 9] had received similar or even lower doses of amiodarone (Table 1) than the patient described by Singhal et al.

While the evidence stands at odds with the authors’ statement that their case represented the first report of severe cirrhosis after low dose amiodarone, it does not preclude the scientific value of the work. That said, there is another important unanswered question. Readers would be puzzled as the authors alluded to the ultrastructural hallmark of lysosomal myelin figures (phospholipidosis) in the Discussion section, and yet failed to mention any electron microscopy finding in the case history. The latter would undoubtedly give weight to the diagnosis (albeit not pathognomonic) of amiodarone hepatotoxicity, as well as distinguishing from alcoholic liver injury.

**Table 1. Case summary of cirrhosis after low dose amiodarone**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Length of treatment (months)</th>
<th>Cumulative dose (g)</th>
<th>Comment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1^</td>
<td>79</td>
<td>33</td>
<td>200</td>
<td>Encephalopathy</td>
<td>Death</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>13.5</td>
<td>165</td>
<td>Encephalopathy, hepatorenal syndrome</td>
<td>Death</td>
</tr>
<tr>
<td>8</td>
<td>83</td>
<td>35</td>
<td>213</td>
<td>Peripheral neuropathy, corneal deposits</td>
<td>Non-fatal</td>
</tr>
<tr>
<td>9</td>
<td>77</td>
<td>12</td>
<td>202</td>
<td>Portal hypertension, inactive hepatitis B</td>
<td>Death</td>
</tr>
</tbody>
</table>

^Case under discussion.
Letters to the Editor

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Reply

SIR—Chow and Liu have raised several points in relation to our case report [1]. First, existence of amiodarone induced liver disease mimicking alcoholic cirrhosis was not claimed to be a new discovery. We have acknowledged the previous work on this subject and reference four of our case report acknowledges the work of Simon et al. [2].

The literature highlighted by Chow and Liu refers to high dose amiodarone therapy leading to cirrhosis and has been referenced as such in our report [2–5]. In contrast our case report is exclusively of low dose amiodarone therapy causing pseudo alcoholic cirrhosis.

Chow and Liu challenge the view that amiodarone induced cirrhosis is rare but failed to provide any reference in their support. They have not provided previous evidence for a lower dose of amiodarone causing cirrhosis nor a reference to this pathology since 1989. They state that the true incidence remains unknown. We find this argument contradictory and in itself supportive of our view of the rare occurrence of this pathology.

Chow and Liu have been confused between daily and accumulative dose. Their reference to an even lower dose of amiodarone causing cirrhosis actually reported amiodarone 400 mg a day for at least 13.5 months [6]. The article referred to 165 g of accumulative dose and not the daily dose. Other listed cases of possible low dose amiodarone causing cirrhosis either had exposure to higher doses of amiodarone or the diagnosis of pseudo-alcoholic cirrhosis was not robust [5].

We agree with the comments that electron microscopic findings would not be pathognomonic of low dose amiodarone causing pseudo-alcoholic cirrhosis and hence see no relevance of its inclusion in our case report.

In conclusion we stand by our published paper [1] and the claim that cirrhosis is an ‘exceedingly rare’ complication of low dose amiodarone therapy.

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