Thyroid dysfunction in long-term amiodarone therapy

Amiodarone is a commonly prescribed medication that frequently causes thyroid dysfunction. Monitoring and treatment of this complication is therefore essential for patients taking long-term therapy.

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Box 1: Side-effects of amiodarone therapy

| Hypothyroidism | Hyperthyroidism | Photosensitivity | Alopeia | Slate-grey skin discoloration | Pulmonary fibrosis | Asymptomatic abnormal liver function tests | Hepatitis | Peripheral neuropathy |

Normal thyroid effects of amiodarone

The normal effects of amiodarone on the thyroid can be subdivided into acute (in the first 3 months of treatment) and subacute (after months; Table 1). In the acute phase, decreased S’diiodase activity contributes to an increase in serum thyroxine (T4) levels and a decrease in tri-iodothyronine (T3) levels. Because of decreased T3 feedback, thyroid-stimulating hormone (TSH) concentrations transiently increase within a few days of starting amiodarone. The level of this hormone usually falls over the next 1–3 months to baseline levels or slightly below. This is known as the Wolff-Chaikoff effect. The subacute phase is characterised by T4 levels in the high–normal reference range (around 40% above baseline), T3 levels in the lower end of normal or slightly below the reference range, and TSH levels as normal.

Amiodarone-induced hypothyroidism

In clinical hypothyroidism, TSH levels are usually >20 mU/l, and T4 levels are usually low. T3 levels are unreliable because the normal physiological response to amiodarone is for T3 to be low. Management depends on the presence of thyroid autoantibodies and whether amiodarone can be stopped. Positive thyroid autoantibodies suggest pre-
Amiodarone-induced thyrotoxicosis

Thyroid-stimulating hormone is low with a normal or raised T4; T3 remains at the lower end of normal. Amiodarone-induced thyrotoxicosis may occur either in the presence of underlying thyroid disease (type I) or in apparently normal thyroid glands (type II). Type 1 is due to iodine-induced excessive hormone synthesis and patients usually have underlying Grave’s disease or multinodular goitre. Ultrasound shows a large hypoechoic and nodular thyroid. The radioactive iodine uptake test shows normal or increased iodine uptake (Table 2).

Type-2 amiodarone-induced thyrotoxicosis

Where amiodarone can be stopped, the mainstay of treatment of type-2 amiodarone-induced thyrotoxicosis is steroids. Typical doses of 40–60 mg prednisolone are used, being trailed off over 3 months. If amiodarone cannot be stopped, then definitive treatment is usually required. This could either be by radio-iodide or subtotal thyroidectomy.
In practice, differentiating between type 1 and type 2 amiodarone-induced thyrotoxicosis is difficult (Table 3). Combined with the fact that many patients go on to require definitive treatment, such as surgery or radioablation, it is recommended that the care of patients with amiodarone-induced thyrotoxicosis involves an endocrinologist.

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying thyroid disease</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ultrasound appearance</td>
<td>Large and hypoechoic</td>
<td>Normal</td>
</tr>
<tr>
<td>Ultrasound appearance</td>
<td>May be nodular</td>
<td></td>
</tr>
<tr>
<td>Radioactive iodine uptake</td>
<td>Normal or increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Is stopping amiodarone effective?</td>
<td>Rarely</td>
<td>Often</td>
</tr>
<tr>
<td>Pharmacotherapy*</td>
<td>Carbimazole (6–9 months while amiodarone is cleared)</td>
<td>Prednisolone (3-month course)</td>
</tr>
<tr>
<td>Definitive treatment in refractory cases or if amiodarone cannot be stopped</td>
<td>Radioactive iodine or subtotal thyroidectomy</td>
<td></td>
</tr>
</tbody>
</table>

*May be successful when amiodarone can be stopped

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Summary

Amiodarone is a commonly prescribed drug, especially in the older population. It is important that health professionals are aware of and competent in managing its side-effects. The high incidence of thyroid dysfunction merits a high index of suspicion when monitoring these patients. The decision of whether to stop amiodarone in those with thyroid dysfunction should be made on an individual basis. The presence of thyroid autoantibodies suggests underlying thyroid dysfunction and a need for definitive treatment. Due to difficulties in differentiating between type-1 and type-2 amiodarone-induced thyrotoxicosis, the care of these patients should involve an endocrinologist. However, it is useful for all physicians to be competent in the monitoring and assessment of thyroid dysfunction in those patients taking long-term amiodarone.

I have no conflict of interest.

References