SNRIs Venlafaxine & Desvenlafaxine
Toxicology

1 Introduction
Venlafaxine and Desvenlafaxine are examples of Serotonin and Noradrenaline Reuptake Inhibitors. Like SSRIs these are commonly prescribed modern antidepressants. However, they pose a much greater risk in overdose compared to SSRIs due to a greater propensity for serotonergic excess and proconvulsant effects. Given these drugs are only available in slow release preparations in Australia, the onset of toxicity can be delayed and overdose warrants a prolonged period of observation.

Toxicokinetics
The oral bioavailability of venlafaxine is 42% as it undergoes significant 1st pass metabolism. Activated charcoal and WBI can decrease its bioavailability appreciably. SNRIs have low protein binding and large volumes of distribution. The half life of venlafaxine is approximately 13 hours. Equivalent doses of desvenlafaxine are ⅔ the dose of venlafaxine therapeutically.

2 Risk Assessment
In overdose SNRIs produce signs and symptoms of serotonin excess, with tachycardia, nausea, vomiting and dizziness. In addition to these more general effects SNRIs are proconvulsant in overdose. The probability of seizures increases with increasing dose. Coingestion of benzodiazepines is protective.

Seizure Probability with increasing dose Venlafaxine

<table>
<thead>
<tr>
<th>Dose</th>
<th>Risk of Seizure</th>
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<tr>
<td>1g</td>
<td>5% (3-8%)</td>
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<tr>
<td>5g</td>
<td>19% (9-35%)</td>
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<tr>
<td>10g</td>
<td>75% (30-96%)</td>
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Seizures occur less commonly with desvenlafaxine. In massive overdose of venlafaxine (>8g), cardiotoxicity with ventricular arrhythmia can occur, which is thought to be due to sodium channel blockade. Similarly a Tako-
Tsubo phenomenon has been reported in massive overdose which may be triggered by high circulating catecholamines. SNRIs does not prolong QT.\(^2\)\(^3\)

3 Management

Decontamination
SDAC and WBI have been shown to decrease the probability of seizures following SNRI overdose. Activated charcoal should be given in consenting patients with significant overdoses (>5g venlafaxine) presenting within 6 hours. WBI should be considered, following intubation and ventilation, in venlafaxine overdoses > 8g given the risk of cardiotoxicity\(^4\).

Supportive Measures
Good supportive care should be the focus of management. Benzodiazepines are necessary to settle symptoms of serotonergic excess or seizures. Large doses may be required.

4 Disposition
As mentioned previously, prolonged observation in this group is necessary due to the risk of delayed symptomatology with the slow release preparation. Most patients require admission under the Toxicology Unit to the short stay ward. If a patient is asymptomatic - with no serotonergic features - 24 hours following ingestion they are suitable for discharge from a medical perspective.

5 Additional Information

- Seizures accompany serotonin excess. Careful serial neurological examinations to assess for serotonin excess, particularly looking for evidence of clonus are crucial.

- Duloxetine is a newer SNRI. A case review of 106 patients has shown it has few serious clinical effects in overdose – causing mild drowsiness and occasional hypertension and tachycardia\(^5\)

6 Further reading


7 References

1. Wikitox Venlafaxine
http://curriculum.toxicology.wikispaces.net/2.1.11.9.2.4.4+Venlafaxine

