INTRODUCTION

Duloxetine (Cymbalta®) is a selective serotonin and noradrenaline reuptake inhibitor (SNRI) with weak activity on dopamine reuptake prescribed for the treatment of major depressive disorder, generalised anxiety disorder, pain related to diabetic neuropathy, and stress urinary incontinence.1

The aim of this work was to review five post-mortem cases, recently submitted to LGC Forensics for toxicological analysis, in which duloxetine, listed as one of the prescribed medications, was detected in the blood.

CASE DETAILS

Case 1: 37-year-old female; found dead in her bedroom. Recent history of self-inflicted injuries. Prescribed medication: duloxetine (Cymbalta® 60mg daily), dlanzapine (20mg daily), chlorpromazine (25mg daily), zopiclone (7.5mg daily), diazepam (dose unknown).


Case 3: 29-year-old male; found hanged. History of depression and mental illness. Prescribed medication: duloxetine, lithium, risperidone.

Case 4: 60-year-old male; found dead with a suspected self-inflicted gunshot wound. Prescribed medication: duloxetine, levethyroxine, minocycline, mirtazapine.


MATERIAL & METHODS

Duloxetine concentrations in blood samples were determined by LC-MS-MS following a liquid-liquid extraction as reported in the following scheme (calibration range 0.001 - 5.000 μg/mL).

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RESULTS

Toxicological investigations were carried out according to customer requests. Results and toxicological interpretation are summarised in the following table.

<table>
<thead>
<tr>
<th>Duloxetine (μg/L)</th>
<th>Toxicological findings of interest</th>
<th>Toxicological interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>0.91</td>
<td>Blood: norepinephrine 0.37 ng/L, chlorpromazine 0.28 μg/L. Duloxetine: higher than levels reported in literature.</td>
</tr>
<tr>
<td>Case 2</td>
<td>0.34</td>
<td>Blood: norepinephrine 0.37 ng/L, chlorpromazine 0.28 μg/L. Duloxetine: higher than levels reported in literature.</td>
</tr>
<tr>
<td>Case 3</td>
<td>0.54</td>
<td>Blood: norepinephrine 0.37 ng/L, chlorpromazine 0.28 μg/L. Duloxetine: higher than levels reported in literature.</td>
</tr>
<tr>
<td>Case 4</td>
<td>0.34</td>
<td>Blood: norepinephrine 0.37 ng/L, chlorpromazine 0.28 μg/L. Duloxetine: higher than levels reported in literature.</td>
</tr>
<tr>
<td>Case 5</td>
<td>0.99</td>
<td>Blood: norepinephrine 0.37 ng/L, chlorpromazine 0.28 μg/L. Duloxetine: higher than levels reported in literature.</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Duloxetine is a relatively new antidepressant medication, introduced in the British National Formulary in 2005. In the recent months an increasing number of Coroner’s cases in which duloxetine was mentioned among the prescribed medications have been recorded in our laboratory (6 cases in a period of 8 months; one was negative for duloxetine, indicating possible non-compliance, and was therefore not reported in the present work).

Of the five cases described in which duloxetine was detected, four had concentrations that were felt as post-mortem therapeutic levels. In Case 1 the concentration of duloxetine appeared to be significantly higher than those recorded in the scientific literature and the verdict at the inquest stated that it was “more likely than not” that the deceased had taken an overdose of duloxetine.

Considering a possible increase in the prevalence of duloxetine prescription, further investigation is required to gain a better understanding of the post-mortem behaviour of this drug. The possible effect of post-mortem redistribution and the potential role of duloxetine in deaths, particularly when taken in combination with other drugs, are of particular concern.

Also, in our experience, the possibility that routine screening procedures (particularly GC-MS in SCAN mode) might not detect duloxetine, unless present at a very high concentration, should be considered.

References