References


Robert Compton
Don Lichti
Dept. of labs.
Barnes Hospital
St. Louis, MO

Jack H. Ladenson
Div. of Lab. Med.
Washington Univ. School of Med.
St. Louis, MO 63110

Poor Responsivity of Qualitative Immunoassay for Tricyclic Antidepressant Drugs in Serum

To the Editor:

Recently, a screening test for toxic amounts of tricyclic antidepressant drugs in serum has been marketed (EMIT®-tox; Syva Co., Palo Alto, CA 94304). When we performed this assay according to the manufacturer's instructions (1), using samples from eight overdose patients with clinical symptoms of overdose and positive urine toxicology screen results for amitriptyline, the results were positive in all eight cases. In two other cases of overdose with chlorpromazine (an assay interferent) and no tricyclics present, the test results were negative. Thus, used on actual patients' samples, the test seemed to serve its intended purpose.

Further analysis suggests that the responsivity and discriminating capability (positive vs negative) may be in question. We performed the assay for various concentrations of drugs in replicates of eight, all of which were run in the same batch on the same day (see Table 1). The cutoff value for interpretation of a positive test is that of the Syva low calibrator (LC; 300 μg/L, as nortriptyline) and the response is measured as the change in absorbance per minute (ΔA/min). For the test to indicate greater than therapeutic (300 μg/L) and possibly toxic concentrations, the low calibrator concentration is set at a reasonable value (2). We find there is considerable overlap between the ranges for the low calibrator and those for the positive test sera. However, discrimination between the low calibrator and the negative sera seems adequate. The responsivity of the test is apparently appropriate for discriminating between undetectable and supratherapeutic (at low calibrator, 300 μg/L) concentrations, but is not appropriate for discriminating between supratherapeutic and higher concentrations.

In one of the overdose patients, for whom only amitriptyline was quantified (1545 μg/L, metabolites not measured), the ΔA/min response was 876. The manufacturer indicates approximately equivalent response to amitriptyline and nortriptyline (1). Although this was a positive response (LC = 826), the assay showed little responsivity for concentrations in this range (300–1545 μg/L). The responsivity for the assay (3) between the LC and the patient's value is 0.04 ΔA/min per microgram per liter, which is similar to the response between the LC and positive control, but the responsivity in the lower concentration range (between negative sera and the LC) is much greater (0.53 ΔA/min per μg/L). Because of this poor responsivity and the overlap in response between the cutoff (LC) value and higher concentrations, I fear that some patients' samples might give a response less than the LC response even though their concentrations might be higher. I suggest that, to increase the response for concentrations above the LC value, Syva might use more enzyme or less antibody in preparing the reagents for this procedure (4).

References


John D. Osterloh
Dept. of Med.
Univ. of California, San Francisco
and
Toxicol. Lab., Ward 35
San Francisco General Hosp.
San Francisco, CA 94110

A representative of the company responds.

Table 1. Responsiveness of EMIT Qualitative Assay for Tricyclics in Serum

<table>
<thead>
<tr>
<th>Drug-free serum (pooled)</th>
<th>Syva neg. calibrator</th>
<th>Syva low calibrator</th>
<th>Syva pos. control</th>
<th>Diluted pos. control*</th>
<th>Patients' samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic present</td>
<td>nor</td>
<td>nor</td>
<td>nor</td>
<td>nor</td>
<td>(n = 8)</td>
</tr>
<tr>
<td>Concentration (μg/L)</td>
<td>0</td>
<td>0</td>
<td>300</td>
<td>1000</td>
<td>500</td>
</tr>
<tr>
<td>ΔA/min</td>
<td>Mean*</td>
<td>638</td>
<td>658</td>
<td>818</td>
<td>844</td>
</tr>
<tr>
<td>SD</td>
<td>14</td>
<td>8</td>
<td>10</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>CV, %</td>
<td>2.3</td>
<td>1.3</td>
<td>1.2</td>
<td>1.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Mean of eight replicates. NA = not appropriate; nor = nortriptyline; dox = doxepin; imi = imipramine; des = desipramine; ami = amitriptyline.

This work was supported by Abbott Labs.