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Letter to the Editor

Effect of blood collection tubes on antidepressant concentrations

Sir,

Serum or plasma antidepressant concentrations may be influenced by the type of collection tube. In particular, blood samples drawn into green-top (heparinized) Vacutainer brand tubes (Becton Dickinson, Rutherford, NJ, U.S.A.) may lead to spuriously low plasma antidepressant levels, presumably because of drug displacement from plasma into red cells by the plasticizer tris(butoxyethyl) phosphate (TBEP) [1-6]. However, the reported extent of plasma level alteration by TBEP is not consistent from study to study. Furthermore, the manufacturer of Vacutainer brand tubes reportedly deleted TBEP from use as a plasticizer [7]. It is also suggested that antidepressant concentrations might differ between serum and plasma, regardless of the collection system [7-9]. The present study was undertaken to compare imipramine and desipramine concentrations between Venoject (Terumo, Elkton, MD, U.S.A.) and Vacutainer brand tubes, as well as between serum and plasma.

EXPERIMENTAL

Eighteen patients chronically taking either imipramine ($n=11$) or desipramine ($n=7$) were recruited via newspaper advertisements and participated after giving informed consent. Via a single venipuncture, blood samples (10 ml each) were drawn consecutively into a Venoject red-top (serum) tube, a Venoject green-top (plasma) tube, a Vacutainer red-top (serum) tube and a Vacutainer green-top (plasma) tube. The sequence of the four tubes was randomized. After collection each sample was inverted several times, centrifuged for 10 min, and the plasma or serum separated and stored frozen in inert polypropylene tubes until the time of assay.

For each patient, serum/plasma concentrations of imipramine and desipramine were determined in duplicate by gas chromatography (GC) with nitrogen-phosphorus detection (NPD) [10]. All samples from a given patient were extracted and analyzed on the same day using the same calibration standards.

TABLE I

INFLUENCE OF BLOOD COLLECTION TUBE ON IMIPRAMINE AND DESIPRAMINE

Values represent mean \pm S.E.; values in parentheses are ranges. N.S. = not significant; d.f. = degrees of freedom.

Blood collection tube	Concentration (ng/ml)	
	Imipramine ($n=11$)	Desipramine ($n=17$)
<i>Plasma</i>		
Vacutainer green	55 \pm 10 (19-123)	101 \pm 20 (9-282)
Venoject green	50 \pm 11 (13-123)	97 \pm 19 (10-319)
<i>Serum</i>		
Vacutainer red	55 \pm 10 (19-118)	96 \pm 20 (10-302)
Venoject red	52 \pm 10 (19-115)	90 \pm 17 (8-271)
Value of F from ANOVA	6.36 ($p < 0.01$) (d.f. = 3,10)	0.54 (N.S.) (d.f. = 3,16)

Differences in imipramine or desipramine concentrations attributable to collection tubes were evaluated by analysis of variance for repeated measures.

RESULTS AND DISCUSSION

For desipramine, small differences were observed in mean concentrations among the four collection systems (Table I). ANOVA indicated that the overall differences were not significant ($F=0.54$). For imipramine, differences of a similar magnitude were observed. Although quantitatively small, the overall differences for imipramine were significant ($F=6.36$, $p < 0.01$).

The present study demonstrated that blood collection into Vacutainer as opposed to Venoject collection tubes, or collection into red-top (serum) versus green-top (plasma) tubes, has at most a small influence on measured imipramine and desipramine concentrations. For both compounds, differences among mean concentrations were no more than 10%, although in the case of imipramine, the overall differences reached statistical significance. Such differences are unlikely to be of clinical importance for therapeutic monitoring of antidepressant therapy unless a patient is at the lower margin of the therapeutic range or has levels bordering on the toxic range. In such cases, therapeutic decisions should be based on clinical findings.

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