Identification and quantification of 30 antipsychotics in blood using LC-MS/MS

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Over the last decade, the prescription rates of antipsychotic (AP) drugs have increased worldwide. Studies have shown that the risk of sudden cardiac death is threefold higher among patients treated with APs. To investigate the presence of APs in postmortem cases, a liquid chromatography (LC)-MS/MS method was developed using only 0.1 ml of blood sample with 10 microl of internal standard (IS) (haloperidol-d(4), 1 microg/ml). After the addition of 0.2 ml of Trizma buffer, the blood sample was extracted using liquid-liquid extraction (LLE) with 1 ml of 1-chlorobutane for 5 min on a shaker at 1500 rpm. After centrifugation at 12,000 rpm for 1 min, the separated solvent layer was transferred to an autosampler vial and evaporated to dryness under N(2). The residue was reconstituted in 0.05 ml acetonitrile containing 0.1% formic acid, vortexed for 30 s and an additional 0.45 ml of 50 mmol/l ammonium formate pH 3.5 was added and the sample vortexed; 0.1 ml of the final extract was injected into a Shimadzu Prominance HPLC system, with detection of drugs achieved using an Applied Biosystems 3200 Q-TRAP LC-MS/MS system equipped with a Turbo V ion source [electron spray ionization (ESI), multiple reaction monitoring (MRM) mode]. The method has been validated according to international guidelines and was found to be selective for all tested compounds. Calibration was satisfactory for all drugs, except olanzapine, from subtherapeutic to toxic concentrations. The lower limits of quantifications (LLOQs) corresponded to the lowest concentrations used for the calibration curves. With the exception of the lowest concentrations of bromperidol, buspirone and perphenazine, accuracy data were within the acceptance interval of +/- 15% (+/- 20% at LLOQ) of the nominal values for all drugs. The method has been proven to be useful for the routine analysis of APs in postmortem blood samples.

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