Oral

[O25-6] O25-6: Drug assay

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[O25-6-4] Development and validation of a high performance liquid chromatography tandem mass spectrometric method for the determination of Docetaxel in dried blood spots

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Background

Docetaxel (DTX) is a widely used anticancer drug characterized by high interindividual variability on drug exposure and narrow therapeutic window. Its use has been associated with potentially severe hematopoietic toxicity, being a potential candidate for therapeutic drug monitoring. Due to its intrinsic stability and handling safety, the determination of DTX in dried blood spots (DBS) can be a good alternative to facilitate sampling and transportation of the samples to reference laboratories. The aim of this study was to develop a method for the determination of DTX in dried blood spots by LC-MS/MS.

Methods

One 8 mm DBS was added with 600 L of extraction solution (methanol:acetonitrile 90:10, v/v) containing IS (docetaxel-D5 6.5 ng/mL) and incubated for 1 hour at 500 rpm/30ºC. The organic layer was evaporated at 45 ºC and resuspended with 100 L of mobile phase containing 10% of 2mM sodium acetate. An aliquot of 25 L was injected on a LC-MS/MS system. Separation was performed in a C18 column (150 x 2.1 mm, 1.7 m) at 30˚ C. Mobile phase was formic acid 0.1% (v/v) and acetonitrile (45:55, v/v) at 0.2 ml min-1. Monitored transitions for quantitation of sodium adducts were 830/549 for DTX and 835/554 for IS. The method was applied to 14 paired clinical DBS and plasma samples.

Results

Retention time was 5,5 min for DTX and IS. The method was linear from 50 to 3,000 ng/mL (y=0.0029x+0.021; 1/x2; r=0.99). Mean DTX recovery was 85%, accuracy 87 to 112%, intra-assay precision 5.83 to 12.06% and inter-assay precision 7.02 to 13.59%. DTX was stable in DBS for 22 days at -20 ºC (93%) and 25 ºC (89%) and 4 days at 45 ºC (88%). Processed samples were stable up to 12 h (CV <12%). The Hct effect (30 to 60%) presented acceptable results with measured concentrations from 91 to 106%. DTX concentrations measured in DBS and plasma samples presented satisfactory correlation (r=0.98, p<0.01).

Conclusions

a LC-MS/MS method for the determination of DTX in DBS was developed and validated. The procedure has adequate analytical performance and can be an efficient tool to optimize DTX treatment.