LC-MS/MS METHOD FOR THERAPEUTIC MONITORING OF AMINOGLYCOSIDES IN CAPILLARY MICROSAMPLES

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INTRODUCTION: Aminoglycosides, such as amikacin (AMI), gentamicin (GEN), and tobramycin (TOB), are widely used antibiotics for the treatment of severe infections, requiring therapeutic monitoring to optimize efficacy and reduce toxicity. Less invasive methods, such as capillary microsampling, have emerged as an alternative to conventional venous blood collection, reducing patient discomfort and allowing for the collection of small volumes of plasma. OBJECTIVE: This study aimed to develop and validate a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for the quantification of aminoglycosides, comparing concentrations between venous and capillary plasma samples. MATERIALS AND METHODS: Capillary plasma samples (20 µL) were prepared using protein precipitation. The method was validated according to FDA guidelines, evaluating linearity, extraction efficiency, and correlation between samples. RESULTS AND CONCLUSION: The calibration curves showed satisfactory linearity for GEN (0.5-50 µg/mL), AMI, and TOB (1.0-100 µg/mL), with $r > 0.99$. The extraction efficiency was greater than 85% for all analytes. A total of 51 paired venous and capillary plasma samples from 13 patients were analyzed, of which 6 were using AMI and 7 were using GEN. TOB quantification was not performed due to the absence of patients undergoing treatment with this drug. AMI concentrations in venous plasma ranged from 13.0 to 62.2 µg/mL (peak) and from 1.5 to 32.1 µg/mL (trough), while in capillary plasma, they ranged from 12.7 to 53.7 µg/mL (peak) and from 1.3 to 29.1 µg/mL (trough). For GEN, concentrations in venous plasma ranged from 3.8 to 6.7 µg/mL (peak) and from 1.5 to 2.2 µg/mL (trough), while in capillary plasma, they ranged from 2.7 to 6.5 µg/mL (peak) and from 1.1 to 2.9 µg/mL (trough). Concentration in paired venous and capillary plasma were highly correlated ($r = 0.980$ for AMI and $r = 0.979$ for GEN). The developed method demonstrated adequate performance and was applied to paired samples, showing a strong correlation between the values obtained in capillary and venous plasma. Thus, capillary microsampling proved to be a viable alternative for therapeutic monitoring of aminoglycosides, contributing to a more comfortable and efficient approach to the clinical management of patients.

Key-words: Aminoglycosides; Therapeutic drug monitoring; Capillary micro-samples; LC-MS/MS.