SALIVA AS AN ALTERNATIVE BIOLOGICAL FLUID FOR THERAPEUTIC DRUG MONITORING OF MYCOPHENOLIC ACID IN RENAL TRANSPLANT RECIPIENTS

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Mycophenolic acid (MPA) is widely used to prevent graft rejection in renal transplant recipients. For MPA therapeutic drug monitoring (TDM), saliva has been investigated as an alternative fluid to plasma (1). The main advantages of saliva are the non-invasive and cost-effective sample collection, permitting more frequent sampling. The purpose of this study was to examine the correlation between plasma and saliva MPA concentrations in renal transplant recipients and the potential of saliva for TDM of MPA. All patients (average age 44.33±11.45 years) were receiving 720-1440 mg/day of MPA (as enteric-coated mycophenolate sodium). Twenty-three paired blood and saliva samples were collected at pre-dose for MPA plasma and saliva trough concentration (C_0) measurement. Both samples were centrifuged at 3000 rpm for 15 min and kept at -80°C until analysis. The MPA plasma C_0 concentrations were determined by the validated high-performance liquid chromatography (HPLC) method (2). The liquid chromatography coupled to mass spectrometry (LC-MS) method was developed for determining MPA in saliva. Mean ± SD of MPA plasma C_0 concentrations (5.24±2.19 μg/mL) in renal transplant recipients was about 100-fold higher than in saliva (55.53±24.75 ng/mL), which could be explained by the fact that the total fraction was analyzed in the plasma, and only the free fraction was assessed in saliva. The average salivary MPA C_0 concentration correlated well with its plasma concentration (r=0.8474). Based on the good correlation between salivary and plasma MPA concentration, saliva can be considered as an alternative to plasma, particularly for unbound MPA monitoring in renal transplant recipients.

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Acknowledgements

The study was supported by Ministry of Education, Science and Technological development of Serbia (grant: 451-03-68/2022-14/200113)

SALIVA KAO ALTERNATIVNA BIOLOŠKA TEČNOST ZA TERAPIJSKO PRAĆENJE MIKOFENOLNE KISELINE KOD PACIJENATA SA TRANSPLANTIRANIM BUBREGOM

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Mikofenolna kiselina (MPA) je jedan od najčešće primenjivanih lekova za prevenciju odbacivanja grafta nakon trasplantacije bubrega. U cilju optimalne imunosupresije, sprovodi se terapijsko praćenje koncentracije MPA u plazmi. Imajući u vidu učestalost uzorkovanja, isplativ i neinvazivan način uzorkovanja, saliva se poslednjih godina sve više ispituje kao alternativa plazmi (1). Cilj ovog istraživanja bio je ispitati korelaciju između koncentracije MPA u plazmi i salivi kod pacijenata sa transplantiranim bubregom i mogućnost primene salive za terapijsko praćenje MPA. Pacijenti sa transplantiranim bubregom (prosečne starosti 44,33±11,45 godine) su primali 720-1440 mg MPA dnevno (u obliku natrijumove soli). Prikupljeno je 23 uzoraka plazme i salive na kraju doznog intervala za određivanje najniže koncentracije (C_0) MPA. Uzorci plazme i salive su centrifugirani na 3000 obrtaja/min, tokom 15 minuta i čuvani na -80°C do analize. Plazma C_0 koncentracije MPA određene su validiranom metodom tečne hromatografije visokih performansi (2). Za određivanje C_0 MPA koncentracije u salivi razvijena je metoda LC-MS (kombinacija tečne hromatografije i masene spektrometrije) sa limitom detekcije 5 ng/mL. Plazma C_0 koncentracija MPA izražena u vidu srednje vrednosti ± standardna devijacija (5,24±2,19 μg/mL) bila je oko 100 puta veća nego u salivi (55,53±24,75 ng/mL), što se može objasniti činjenicom da je u plazmi analizirana ukupna frakcija, a u salivi slobodna frakcija MPA. Prosečna C_0 koncentracija MPA u salivi je u dobroj korelaciji sa plazma koncentracijom (r=0,8474). Dobra korelacija između C_0 koncentracija MPA u salivi i plazmi omogućava da se saliva primenjuje kao alternativa plazmi, posebno za praćenje slobodne frakcije MPA kod pacijenata sa transplantiranim bubregom.

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Zahvalnica

Rad je rezultat istraživanja koje je finansiralo Ministarstvo prosvete, nauke i tehnološkog razvoja Srbije (451-03-68/2022-14/200113).