
Symposium

[S-18] S-18: TDM for cardiovascular and endocrine diseases

Chairs: Hirotochi Echizen, Japan / Naoki Matsumoto, Japan

Wed. Sep 27, 2017 10:30 AM - 12:00 PM Room E (1F)

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[S-18-3] Development of a dried blood spot (DBS) based measurement of eight antihypertensive drugs and four active metabolites to assess treatment adherence

Jorie Versmissen¹, Edon Hameli², Soma Bahmany³, Tom Zwart⁴, Bart Van Der Nagel⁵, VanDenMeiracker Anton⁶, Teun van Gelder⁷, Birgit Koch⁸ (1.Erasmus MC, Rotterdam, The Netherlands, 2.Erasmus MC, 3.Erasmus MC, 4.Erasmus MC, 5.Erasmus MC, 6.Erasmus MC, 7.Erasmus MC, 8.Erasmus MC)

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Background

Non-adherence to antihypertensive drugs is a common health issue leading to suboptimal cardiovascular prevention. Proving who is adherent and who is not can be difficult while this is an important first step before non-adherence and ways to improve adherence can be discussed. We aimed to develop a method to measure drug levels of eight of the most commonly used antihypertensive drugs in DBS.

Methods

We developed a rapid multimethod using UPLC-MS/MS for eight antihypertensive drugs and four active metabolites in plasma and DBS: enalapril (and metabolite enalaprilate), perindopril (and perindoprilate), losartan (and losartan carboxylic acid), valsartan, hydrochlorothiazide, spironolactone (and canrenon), amlodipine and nifedipine. Both plasma and DBS methods were validated according to FDA guidelines. For further clinical validation, we measured peak and trough levels in both DBS and plasma from patients assumed to be adherent (based on blood pressure below target value), aiming for 10 patients/drug.

Results

Validation using standard concentrations in blank human plasma and blood showed high linearity between plasma and DBS measurements within a hematocrit range of 0.3-0.5. So far, peak and trough levels in plasma and DBS were measured for a total of 6-14 patients per drug. Trough levels in plasma were below LLOQ (lower limit of quantification) for spironolactone, enalapril, perindopril and hydrochlorothiazide but for the first three the levels of the active metabolites were above LLOQ. LLOQs were on average 10 times higher for the DBS methods than for plasma measurement. However, using DBS, drug levels or an active metabolite for all drugs except hydrochlorothiazide could be detected at least 24 hours (hydrochlorothiazide: six hours) after intake above the lower limit of detection (LLOD) which is most important for assessing (non-)adherence at a random time point.

Conclusions

Therapeutic drug monitoring using DBS can be a convenient method to monitor drug adherence of antihypertensive drugs. The advantage of DBS above plasma measurements is that sampling can take place at the exact moment the increased blood pressure is measured, for instance in the physician's office. When more exact analyses of drug levels are desired plasma measurement is more accurate at lower concentrations.

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