Validation of the new CEDIA THCplus urine immunoassay

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AIMS: It has become common practice in different therapeutic settings to monitor abstinence from cannabis with semiquantitative immunoassays in urine samples. It is often assumed that these tests are monospecific and do only crossreact with the main metabolite 11-nor-9-Carboxy-delta-9-Tetrahydrocannbinol-glucuronide (THCCOOH) and that dilution of a high positive sample can be used to extent the measuring range. This is needed because of the narrow measuring range of the tests. However, this may lead to problems due to inter- and intra-individual variability in metabolite pattern and when patients results are compared with tests from different manufacturers even at the same cutoff. In this study we wanted to compare the new CEDIA THCplus with an extended measuring range with two established immunoassays and with GC/MS.

METHODS: Firstly, 102 fresh urine samples from 72 patients in substitution therapy were randomly selected and analysed with FPIA on an Axsym (Abbott) and consecutively on an Olympus AU640 with CEDIA THC and CEDIA THCplus (Microgenics). Assays were performed according to the manufacturer. Calibration curve was third order polynomial for the FPIA (0, 25, 40, 60, 80, 135ng/mL), polygonal for the CEDIA THC (0, 13, 25, 50, 75, 100ng/mL) and "EIA-Type1" for the CEDIA THCplus (0, 25, 50, 100, 200ng/mL). Samples above the measuring range were reanalysed with FPIA and CEDIA THCplus after 1:10 or 1:100 dilution with 0.9% saline. Applied cutoff was 25ng/mL for all assays. Intra- and interassay variability of the CEDIA THCplus were studied with control material provided by Microgenics. Subsequently, 55 randomly selected fresh urine samples from 55 patients in substitution therapy were run with the CEDIA THCplus as described above and also by GC/MS. GC/MS was performed from 1mL alkaline hydrolyzed sample with a validated method (LOD: 1.1ng/mL, LOQ: 3.6ng/mL).

RESULTS: CEDIA THCplus intraassay (n=10) gave RSD from 2.2% to 5.2% at 6 different THCCOOH levels. Interassay on 5 consecutive days (n=30) gave RSD from 2.2% to 7.8%.
From the 102 samples 6 samples were negative with all assays, but CEDIA THCplus gave additional 7 (CEDIA THC: 2) negative results which were shown by GC/MS to contain THCCOOH (9.4-12.5ng/mL). CEDIA THC gave 3 false positive results (53-70ng/mL) which was due to 8-hydroxy-efavirenz-glucuronide. In CEDIA THCplus 57samples (56%) were found in the measuring range and 32(31%) samples were above. In FPIA: 46 samples (45%) were in the measuring range and 50(49%) above with 4 samples >1350ng/mL; CEDIA THC: surprisingly 55 samples (54%) were in the measuring range and only 39 samples >100ng/mL. Regression analysis of FPIA versus CEDIA THCplus gave the best correlation in the 0-800ng/mL range (r2: 0.97, slope: 1.12, intercept: 24). Correlation to the CEDIA THC would have been possible only in the 0-60 ng range because of beginning non-linearity. From 50 samples, which were >100ng/mL in the CEDIA THCplus 13 samples were within the measuring range in the CEDIA THC.

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From the 55 samples series, 21 samples were negative with the CEDIA THCplus but 7 contained THCCOOH (1.9-6.0ng/mL). On the other hand from 11 samples below 15ng/mL THCCOOH in GC/MS, 4 were positive with CEDIA (34-84ng/mL). CEDIA positive samples in the measuring range were 8 while 26 samples were >200ng/mL. Correlation of CEDIA with GC/MS values gave the following: range 0-2000ng/mL: slope 1.7, r^2 0.64 and 0-200ng/mL: slope 3.8, r^2 0.82.

CONCLUSIONS: The CEDIA THCplus is not crossreacting with efavirenz-metabolites. It shows a good correlation even after dilution with the FPIA but seemed to be less comparable with the old CEDIA when quantitative results were regarded. As expected from studies with other THCCOOH assays, correlation with GC/MS esp. after diluting the sample, is again not satisfactory for patient follow up.

KEYWORDS: *CEDIA THCplus, THC FPIA*

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