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URINARY PROTEOME ANALYSIS BY CAPILLARY ELECTROPHORESIS COUPLED MASS SPECTROMETRY (CE-MS) FOR DETECTION OF TENOFOVIR-ASSOCIATED KIDNEY DAMAGE IN HIV PATIENTS

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BACKGROUND: Treatment with tenofovir has been associated with renal dysfunction. Monitoring of early renal impairment is often based on indirect or complex direct measurements of kidney function. As physicians and patients are concerned about potential renal long term toxicities of tenofovir therapy, new technologies for early kidney damage assessment should be explored.

OBJECTIVE: To compare the urinary polypeptid pattern obtained by proteome analysis of patients with increased serum creatinin during tenofovir-containing HAART ($n=11$, group 1), patients on tenofovir-containing HAART with normal serum creatinin ($n=15$, group 2), patients receiving HAART but no tenofovir ($n=10$, group 3), and therapy-naïve HIV-patients ($n=14$, group 4).

METHODS: On-line combination of capillary electrophoresis and mass-spectrometry (CE-MS) to obtain data on urinary polypeptides and comparison with data sets of defined kidney diseases and healthy controls.

RESULTS: In group 1 the mean creatinine had increased from $79 \pm 15 \mu\text{mol/l}$ (before tenofovir therapy) to $114 \pm 11 \mu\text{mol/l}$ ($P < 0.001$) corresponding to a 25% increase. Mean serum creatinine in group 2 had increased from $66 \pm 11 \mu\text{mol/l}$ to $74 \pm 13 \mu\text{mol/l}$ (14%; $P < 0.001$) but mean creatinine remained normal ($< 80 \mu\text{mol/l}$). Patients of group 1 were significantly longer on antiretroviral therapy (94 ± 17 months) compared to group 2 (63 ± 38 months, $P = 0.032$). Time on tenofovir comparable between group 1 and 2 (27 ± 10 months versus 21 ± 11 months, $P = 0.13$). Calculated creatinine clearance decreased significantly by 33% in group 1 ($111 \pm 42 \text{ ml/min}$ to $74 \pm 20 \text{ ml/min}$; $P = 0.002$). In group 2

the mean calculated creatinine clearance decreased by only 10% from 126 ±44 ml/min to 112 ±48 ml/min ($P=0.002$). Urinary proteom analysis revealed that 73% of patients in group 1 had a pathological polypeptide pattern defined by comparison with a data set of various kidney diseases and healthy controls. Interestingly, 67% of patients receiving tenofovir but having normal serum creatinine (group 2) presented a pathological urinary polypeptide pattern. In contrast, only 20% and 21% patients of group 3 and 4 were diagnosed with a pathological urinary proteome analysis.

CONCLUSION: Tenofovir therapy was associated with pathological urinary polypeptide patterns independent of pathological serum creatinin increase or reduced calculated creatinine clearance. CE-ME may aid in early diagnosis and discovery of the pathogenetic background of tenofovir-associated kidney damage.

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