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EARLY MARKERS OF ACQUIRED FANCONI'S SYNDROME ASSOCIATED WITH TENOFOVIR THERAPY IN CHILDREN

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Introduction: A resorptive abnormality in the proximal tubule of the kidney known as Fanconi syndrome (Fs) can be brought on by certain drugs, cystinosis, Lowe's syndrome, or Wilson's disease. Nucleoside reverse transcriptase inhibitors, chemotherapeutic agents (cisplatin), immunosuppressives (azathioprine), antibiotics (gentamicin), or several other drugs can all cause secondary Fs, an acquired condition. Amino aciduria, low molecular weight proteinuria, hypophosphatemia, metabolic acidosis, glycosuria, and a rise in parathyroid hormone are some of the clinical symptoms of FS. The values of these criteria are not specific to proximal tubular defects.

Aim This study aims to demonstrate the early specific biochemical markers of Tenofovir Disoproxil Fumarate (TDF) induced Fs.

Materials & Methods: - We thoroughly analyzed 26 abstracts and case studies from the last 5 years using PubMed & MeSH ,we reviewed modern scientific literature of all the associated medications their biomarkers and their significance in secondary Fs. Around 30% of those were pediatric cases. Rest 70% were non pediatric cases. However, they provided an insight about all the early biochemical markers that if detected early can be more specific and hence would prevent permanent damage to kidneys and help in early diagnosis.

Results- We found that estimated Glomerular filtration rate (GFR) (18 studies) and urine creatinine/ albumin ratio (18 studies) were increased they are specific for kidney damage however not specific for proximal tubule defects.

For earlier detection of TDF-associated tubular toxicity Urine α1-microglobulin (A1M) (3 studies), a low-molecular-weight protein was used

Urinary proteomics (1 studies) were present in high concentration in the nephron of patients with tubular proteinuria, with nanoflow liquid chromatography and tandem mass spectrometry (nanoLC-MS/MS) urinary peptides were analyzed and over 100 molecular species were detected apart from which there were also some novel proteins and potentially bioactive peptides which are not present in normal urine.

Urinary excretion of β2m (3 studies), NAG (5 studies), Clara cell protein (CC16) (1 study).

Patients with elevated levels of retinol-binding protein and beta-2-microglobulin have been linked to mitochondrial dysfunction brought on by tenofovir in one research. Both biomarkers might be helpful for identifying proximal tubular toxicity, whether they are used in conjunction with other tubular parameters or alone.

Other molecules, such as urinary kidney injury molecule- 1(4 studies), neutrophil gelatinase associated lipocalin (1 studies), or N-acetyl-b-D-glucosaminidase are also an important biomarker in early detection.

Conclusion

Urine α1-microglobulin (A1M), Urinary proteomics, β2- microglobulin, NAG were shown to have high specificity for drug induced Fs and were raised early in all the 3 studies. Hence, they can be considered specific for proximal tubular toxicity and early biomarkers for Fs associated with TDF.

Keywords - Fanconi syndrome, tenofovir and biochemical markers

References:

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