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P400 -CHARACTERISING FUMADERM-INDUCED FANCONI SYNDROME: A CASE SERIES

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BACKGROUND: Fumaderm, a fumaric acid ester, is prescribed for chronic plaque psoriasis. Fumaric acid esters have been linked to drug-induced Fanconi syndrome. Fumarate is an important component of the Krebs cycle, and hence the production of ATP. Proximal tubular cells have a high ATP demand due to their role in actively transporting molecules from the filtrate. It is thought that fumaric acid esters are toxic to mitochondria, but until now there has been little published on this.
METHODS: We describe a case series of 10 patients with Fumaderm-associated Fanconi syndrome diagnosed and managed at a tertiary tubular clinic. Patients were investigated with serum and urine biochemistry. 5 patients had a renal biopsy with examination of the specimens by electron microscopy.
RESULTS: 70% of the cases were men; the median age was 36.5 years (IQR 32.25-54.25). The most common ethnic group was white British (50%). The median dose of Fumaderm was 600mg (IQR 360-720mg). The median RBP at presentation was 8385µg/ml (IQR 2793-14600µg/ml) and RBP:creatinine ratio was 710 (IQR 390-2415). All patients had a low serum phosphate, with a median value of 0.86mmol/L (IQR 0.08-1.01mmol/L), and as expected all patients had a grossly elevated fractional excretion of phosphate (median 169%, IQR 134-196%). Serum urate values were also low (median 150µmol/L, IQR 145-190µmol/L). Electron microscopy of the renal biopsies showed mitochondrial damage. While most patients stopped the drug or were managed at lower doses, 3 patients went on to be treated with probenecid, with an excellent biochemical response in 2 (the third patient terminated treatment after a severe skin reaction).
CONCLUSIONS: Here we demonstrate that the Fumaderm-associated Fanconi syndrome is associated with mitochondrial damage visible on electron microscopy. In cases where it is not appropriate to stop Fumaderm or lower the dose, this effect can be mitigated by blocking the organic anion transporter with Probenecid, which prevents delivery of the drug to the mitochondria.