EVALUATION OF SERUM LEVEL OF OSTEOPONTIN (Eta-1) IN UREAMIC PATIENTS WITH PRURITIS

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SUMMARY

Uremic pruritis remains one of the most frustrating, common and potentially disabling symptoms in patients with end-stage renal disease. It affects 15%-49% of patients with predialysis chronic kidney disease and 50%-90% of patients on dialysis including peritoneal and hemodialysis. It occurs more frequently in patients on dialysis for more than 3 months ***(Narita et al., 2008).***

Several hypotheses have been postulated for the possible etiology underlying the development of uremic pruritis, but none is conclusive. Uremic pruritis is thought to be the consequence of a complex contribution of many uremic and nonuremic factors ***(Lara and Makram, 2012).***

Several factors are proposed to play a role in the pathogenesis of UP but a specific general etiology has not been determined. Metabolic abnormalities such as secondary hyperparathyroidism, hyperphosphatemia with increased calcium phosphate deposition in the skin and increased calcium/phosphate product, histamine release by mast cells, alterations in the endogenous opioidergic system with overexpression of opioid l-receptors and anemia (or possibly some other manifestation of erythropoietin deficiency) have been suggested to contribute to the development of UP; however, not all these findings were confirmed by subsequent studies ***(Fallahzadeh et al., 2011).***

It appears that UP is a systemic inflammatory disease rather than a local dermatologic disorder. Dearrangement of T helper cells balance with TH1 predominance appears to be a major contributor to this systemic inflammation. TH1 cells produce inflammatory cytokines such as interferon-gama that recruit and activate leukocytes; therefore, the overactivity of TH1 cells results in an inflammatory response. On the other hand, TH2 cells

secrete anti-inflammatory cytokines such as interleukin (IL)-4 and are associated with allergic responses ***(Abbas et al., 1996).***

Osteopontin also known as early T lymphocyte activation 1 (Eta-1), is a phosphorylated acid glycoprotein firstly identified as a bone component involved in bone formation and calcification. It is secreted by osteoblasts, lymphocytes, macrophages, keratinocytes, and vascular smooth cells. Osteopontin is also implicated in cell-mediated immunity, cell survival, inflammation, and tumor invasion and Metastases ***(Ganzetti et al., 2015).***

Following activation, naïve CD4 T cells can differentiate towards Th1, Th2, or Th17 cells which differ in effector function. The development of Th1 cells leads to cell mediated immunity while development of Th2 cells provides humoral immunity. Th17 cells are associated with autoimmunity. OPN is upregulated in response to T cell receptor ligation. OPN functions in T cells by mediating migration, adhesion, and co-stimulating T cell proliferation ***(Lund et al., 2009).***

High circulating OPN levels have been reported in several dermatological and non-dermatological diseases, Therefore, given the role of osteopontin in Th1- mediated inflammation ***(Ganzetti et al., 2015).***

The aim of this study is to investigate the serum level of osteopontin in uremic patients with and without pruritis and its comparison with controls, in an attempt to elucidate its role in the pathogenesis of itching in renal failure patients undergo heamodialysis which might help in treatment.

Fifty nine patients with renal failure undergo heamodialysis were recruited from Department of Nephrology at El-Fayoum University Hospital (the study was performed in 6 months duration: from April 2016 to September 2016).

Patients were divided into 3 groups:

- Group 1: 30 patients with renal failure and undergo hemodialysis, complaining of itching (RF+ heamodialysis+ itching).
- Group 2: 29 patients with renal failure and undergo hemodialysis, but not complaining of itching (RF+ heamodialysis).
- Group 3: 19 normal persons without renal failure (Normal).

Patients with HBV or HCV or other skin diseases were excluded from study, Informed consent was obtained from all subjects.

Serum samples were processed from whole blood, stored in aliquots at -80°C and used after thawing osteopontin (Cusabio, china) measurement using commercially available ELISA kits according to the manufacturer's recommendations.

There were 24 patients with RF and itching (80%) and 8 patients with RF but no itching (31%) and 1 control (5,2%) with significant high level of osteopontin in serum.

In this study we measure serum level of osteopontin in patients with RF and undergo heamodialysis and we find it is significantly high in renal patients complaining of itching ($P<0.001$) test with high mean among group I with itching (17.4) and lower among group II (5.6) and the lowest level among controls (0.80). This work is unique for our literature, no previous literature measure osteopontin in renal failure patients. We try to detect if high level of osteopontin in renal patients may contribute to itching in these patients or not.