UREMIC PRURITUS AETIOLOGY AND MANAGEMENT

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Abstract:
Pruritus begins in patients undergoing hemodialysis or peritoneal dialysis after about six months of the beginning of dialysis. The mechanism of pruritus is not clear and some underlying factors were considered and include secondary hyperparathyrodism, increased number of mast cells, increased histamine, neuropeptide (substance P), hypoferritemia, Zinc deficiency and hyervitaminosis A. The therapies tried with variable degrees of success are phototherapy, phosphate binding agents, erythropoietin, ketotifen, nicergoline, cholestyramines, antihistamines, activated charcoal, dietary restriction, efficient dialysis and the use of non-complement activating dialysis membranes, emolients, topical steroids and electric acupuncture.

Uremic pruritus is a significant problem seen in 70% of patients with end stage renal failure[1]. The underlying mechanism of uremic pruritus remains unknown, Most patients maintained on hemodialysis have pruritus and secondary hyperparathyroidism and high level of parathyroid hormones is a common finding in such patients. The role of the parathyroid hormone (PTH) in uremic pruritus was studied and it was found that the serum levels of PTH did not correlate with the intensity of pruritus[2]. In the same study it was concluded that substance P may act as a neurotransmitter and topical copsaisin can be used for localized uremic pruritus[2].

End stage renal failure patients with pruritus had more numerous degranulated mast cells in the skin and had significantly low serum iron and high levels of histamine[3]. Favourable therapeutic effects were achieved with iron supplementation in those patients with hypoferritemia or with antihistamines and mast cell stabilizers[3]. Serum zinc was found to be decreased in uremic pruritus while serum histamine increased[4]. Zinc has an inhibitary role in releasing histamine from mast cells. So it is suggested that zinc deficiency participates in increased histamine levels in dialysis patients and subsequently in development of uremic pruritus. Oral zinc sulfate 445mg daily relieved pruritus in 53% of patients[4]. Uremic pruritus may be due to increased skin divalent ion content resulting in microprecepitation of calcium or magnesium phosphate[1]. Skin biopsies obtained from all pruritic patients revealed elevated contents of calcium, magnesium and phosphorus. The resolution of pruritus following UVB treatment was associated with reduction of skin phosphorus comparable with healthy volunteers[1]. Abnormalities in plasma composition of essential fatty acids (EFAs) may be aetiological in uremic pruritus. Evening primrose was tried to treat patient with uremic pruritus with promising result. It shifts eicosanoid metabolism towards a less inflammation status through modifying plasma concentrations of their precursor n-6 EFAs[5].

Serotonin and histamine have been reported as possible mediators of uremic pruritus. Ondansetron is a potent and selective inhibitor of serotonin type 3 receptors and is a safe well tolerated and effective treatment of uremic pruritus[6]. The dose is 8mg per day till improvement then 8mg per week thereafter, Serotonin does not only act on histamine containing mast cells but has its own pruritic potency[7].

Mild localized or severe generalized pruritus starts in 50-90% of patients undergoing peritoneal dialysis or hemodialysis after six months after the start of the dialysis[8].

The most effective treatments currently available are efficient dialysis, dietary restrictions, phosphate binding therapy and phototherapy[8].

Oral activated charcoal 6grams daily was found safe and effective in uremic pruritus[9]. Its mechanism of action is unknown. Patients under hemodialysis showed significantly higher values of leukotriene B4 and C3a compared to healthy non hemodialysis subjects. Two mg per day of azelastin hydrochloride which is an anti-allergic drug was orally given to patients with uremic pruritus for 3 weeks. The level of leukotriene B-4 was significantly reduced in all patients whether the pruritus improved or not. Therefore leukotriene B4 activity did not seem to be related to development of pruritus[10]. Highly efficient dialysis with good nutritional state reduces the prevailing and degree of pruritus in hemodialyzed patients[11]. Thalidomide was effective in controlling uremic pruritus[12].

Patients with uremic pruritus have elevated plasma histamine and erythropoietin given in the dose of 36-18 units per kg three times weekly decreases plasma histamine level and results in marked improvement of pruritus[13].

Ultraviolet B phototherapy is the treatment of choice to severe uremic pruritus[14]. Uremic pruritus improved dramatically during or after electrical needle stimulation therapy[20].

References :

1- Blachley-JD; Blankenship-DM; Menter-A et al: Uremic pruritus : Skin divalent ion content and response to ultraviolet

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