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Pruritus and Renal Failure

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Patients with renal failure, usually end-stage renal disease (ESRD), commonly are afflicted by severe pruritus. The pathogenesis of ESRD pruritus is unknown, but improving the quality of dialysis can reduce the prevalence and severity of ESRD pruritus. Topical and systemic agents as well as broadband ultraviolet phototherapy can be extremely beneficial. Gabapentin has been recently discovered as an effective agent for the patient with ESRD pruritus. Kappa opiate agonists are promising new therapeutic options.
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Pruritus is a common symptom in patients with end-stage renal disease (ESRD). In older series, up to 90% of patients were afflicted with pruritus, but now between 20% and 50% are affected.[1-3] Pruritus occurs independent of the cause of the ESRD, and patients on both peritoneal and hemodialysis experience pruritus at similar rates. All races, both genders and all ages can develop ESRD pruritus.[4] Nephrologists have recognized and documented significant impact of itch on ESRD patients' quality of life. In addition, pruritus is an independent predictor of increased mortality, probably because of effect on a patient's quality of sleep.

The pathogenic basis of pruritus in renal failure is unknown. The renal failure must be severe to be associated with pruritus. The resolution of itch, albeit slowly in some cases, after renal transplantation suggests that a factor normally removed by the kidney but not effectively removed during dialysis is playing a role. Xerosis is common in patients with ESRD and may contribute to pruritus. ESRD pruritus is associated with elevated C-reactive protein and other inflammatory cytokines, suggesting there is an inflammatory component in this form of pruritus. The abnormalities of calcium metabolism that occur in the setting of ESRD may lead to formation of calcium phosphate crystals in the skin. These crystals may stimulate itch receptors. As in hepatic pruritus, endogenous opioids may be important in mediating the itch associated with ESRD. Once chronic pruritus has occurred, there may be secondary changes in nerves in the skin and perhaps the central nervous system which enhance the perception/sensation of itch (central sensitization).

The clinical characteristics of ESRD pruritus are variable.[1] The pruritus may be constant or intermittent. The back is the most commonly affected area, but arms, head, and abdomen are also commonly affected. Excoriations with no primary lesions, and sparing of the butterfly area of the back are typical. Patients with ESRD, especially if attributable to diabetes mellitus, frequently develop keratotic nodules that on biopsy show a perforating disorder. These represent prurigo nodules and are a marker for severe and long-term pruritus.

The therapy for renal pruritus is often rewarding because the dermatologist has numerous options, some of which are usually effective. Treatment begins with topical agents. Treatment of xerosis with moisturization and gentle skin care can be quite beneficial.[5] The addition of soothing topicals containing menthol or pramoxine can be tried.[6] Topical capsaicin can also be beneficial for patients with localized pruritus. Topical tacrolimus dramatically reduced pruritus by 80% in one study of patients with ESRD pruritus, but the vehicle gave a similar result.[7] For localized pruritus, this could be considered as an option, but for widespread itch, systemic absorption and cost are limitations.

Standard first- and second-generation antihistamines are usually of limited value. However, doxepin 10 mg once or twice daily has been shown effective.[8] Blood levels can be monitored enhancing safety. Mirtazepine 15-30 mg/d is another option. Both montelukast and cromolyn sodium, agents used in allergic disorders, have shown efficacy in ESRD pruritus.[9,10]

Adequate and effective dialysis is critical in alleviating pruritus in ESRD.[10] Controlling calcium and phosphorus seems to be particularly important.[11] In addition, treating the underlying iron deficiency may alleviate itch.[12]

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The administration of 300 mg of gabapentin after each dialysis has been shown in multiple studies to improve ESRD pruritus.[13] The response to treatment, although not universal, is usually durable, and when effective is a very safe new addition for the treatment of ESRD pruritus. Pregabalin can be similarly effective.[14]

Ultraviolet B (UVB) phototherapy, especially broadband UVB, is frequently effective for ESRD pruritus.[15] NB–UVB and UVA alone do not appear as effective. Starting at three times per week and reducing to maintenance once or twice weekly can often control the pruritus.

The standard opiate antagonists naltrexone and butorphanol can be tried but have not been universally beneficial. Nalfurafine, a kappa agonist, demonstrated modest improvement and is a potential new option for treatment of ESRD pruritus.[16]

In refractory patients, novel approaches may be useful. The administration of 1 mg of ganisetron orally twice a day can be effective, but another serotonin type 3 receptor antagonist, ondansetron, is ineffective.[17] The administration of 600 mg of pentoxyfilline once after each dialysis, although poorly tolerated by some patients, was reasonably effective in a small series.[2] Thalidomide at a dose of 100 mg daily has reduced pruritus rapidly in one series and should be considered in refractory patients, especially those with prurigo nodules.[18] In the most severely affected patients, 5 mg of nicergoline intravenously during dialysis can be tried.[3] Acupuncture and other physical modalities may provide benefit.[1,19]

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