Complement Inhibition in Kidney Disease

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However, the clear benefit of avacopan treatment at 26 weeks is the sparing of high doses of steroids and subsequently avoidance of glucocorticoid-related toxicity (8).

The exciting part of complement inhibition in glomerular diseases is ongoing, and new therapeutic strategies targeting other parts of the complement cascade, such as C3, factor B, factor D, and C1, are currently under various stages of basic and clinical development. ■

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Treatment of Uremic Pruritus

By Swetapadma Tripathy, and Jia Hwei Ng
Visual abstract by Jia Hwei Ng, MD

Uremic pruritus is a common, distressing condition that affects 60% of patients on hemodialysis (1, 2). Despite the high prevalence, this condition is under-recognized by physicians, and high-quality evidence on the treatment options is limited (3). Here, we summarize a recent narrative review on non-pharmacological and emerging pharmacological treatment options to treat uremic pruritus (4). We will highlight the therapies where randomized controlled trials (RCTs) were conducted (see visual abstract).

Optimization of dialysis and bone mineral disorder

Given that uremic toxins likely contribute to the symptoms of uremic pruritus, increasing dialysis dose (increased Kt/V) and using a high-flux dialyzer result in moderate improvement of symptoms (5). In addition to dialysis, optimization of the bone mineral disorder, along with parathyroidectomy, improves symptoms through the reduction of a calcium-phosphate product (6).

Topical agents

Patients with kidney failure commonly have dry skin, contributing to itchiness. Emollients are effective in reducing xerosis and reducing pruritus symptoms. Capsaicin and pramoxine have been used, but evidence on their efficacy is limited to a few RCTs with small sample sizes (5). Topical tacrolimus suppresses immune-mediated exacerbation of dry skin, inflammation, and pruritus. Despite its potential for treating uremic pruritus, an RCT showed its lack of efficacy in patients on hemodialysis (7). Additionally, there is a US Food and Drug Administration (FDA) warning on the risk of dermatological malignancies with the use of topical tacrolimus (8).

Systematic pharmacological interventions

Mast cell stabilizers block effects of histamine to reduce itch; however, evidence on their effectiveness has been conflicting (5). Gabapentin and pregabalin are the most widely studied medications for uremic pruritis, and both have been shown to be effective (5). They work by negatively modulating voltage-gated calcium channels and calcitonin gene-related peptide release. Some patients report dizziness and somnolence as side effects. Thus, extra caution has to be made to adjust the dose of gabapentin and pregabalin according to a patient's kidney function (9).

Opioid receptor modulators

More recently, clinical trials on opioid receptor modulators to treat uremic pruritus have been emerging. Based on current literature, the μ-antagonist promotes pruritus, whereas the κ-receptor inhibits pruritus. μ-Antagonists, such as naltrexone, have been found to be ineffective in RCTs; additionally, they come with adverse effects, such as sedation and gastro-intestinal complications (10, 11). κ-Receptor agonists are more favorable options than μ-antagonists, as κ-receptor agonists do not promote euphoria. Nalfurafine is the selective central activation of the κ-receptor, which contributes to anti-itch sensation; however, it is only approved for use in Japan (12, 13). Difelikefalin is a peripheral κ-receptor that does not penetrate the blood-brain barrier. In the recent phase 3 randomized clinical trial, difelikefalin showed increased effectiveness in reducing pruritus symptoms compared to placebo (14). Its adverse effects include diarrhea, dizziness, and vomiting. Difelikefalin is not yet approved by the FDA for use. Finally, nalbuphine, a dual κ-receptor agonist/μ-antagonist, has been studied in opioid-related pruritus but not widely studied in uremic pruritus. So far, one clinical trial showed that nalbuphine reduced the intensity of itchiness among patients on hemodialysis (15). Currently, nalbuphine is only approved by the FDA for use for analgesia, not for itching (16). ■

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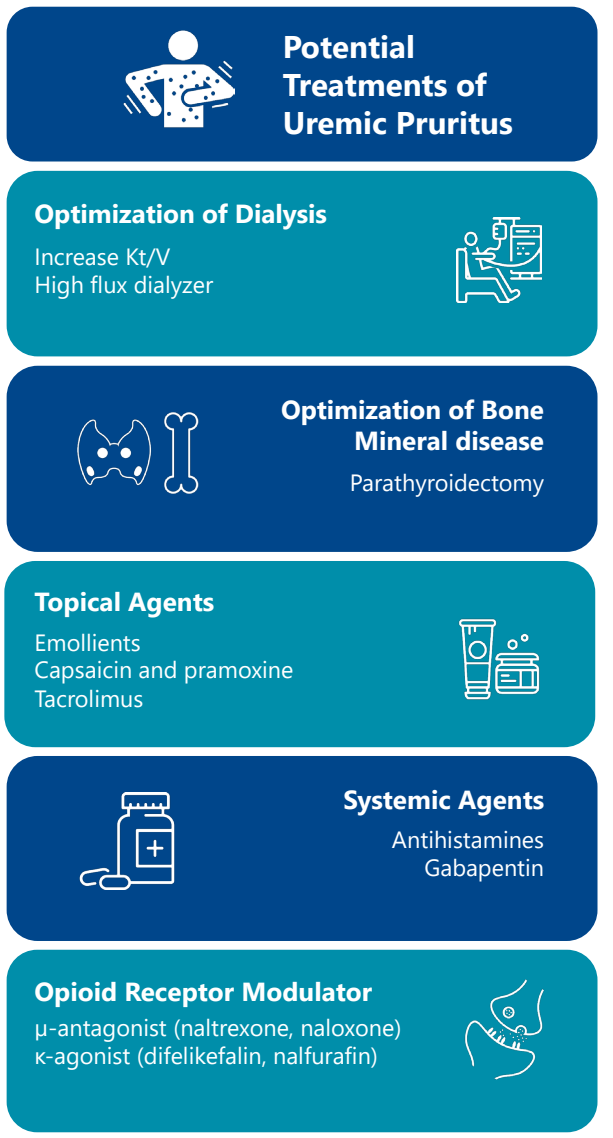

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