guidelines and methodology for such studies and for these to be incorporated into national and international standards.

When selecting a device, the potential purchaser is interested not only in the performance of the device, but also in how it compares with other similar devices. To permit such comparison the purchaser needs to have access to comparative data established in accordance with a well-defined and validated protocol. Such protocols do not form part of international and national standards, and to avoid the necessity of each purchaser undertaking 'mini' evaluations, authoritative data such as that generated by the United Kingdom’s Medical Device Agency’s Evaluation Programme should be considered.

References

Pruritus in dialysis patients: a neglected problem

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What is pruritus?

Pruritus has been defined as a poorly localized, unpleasant sensation which elicits the desire to scratch. Pruritus has often a psychological origin. Probably the reader remembers how many students scratched themselves while the professor of dermatology demonstrated a patient suffering from severe itching! Fortunately, psychogenic pruritus can be overcome in few seconds by most subjects, although pathological forms of psychogenic pruritus are well recognized and can be difficult to treat. In clinical medicine pruritus may be a symptom of skin disorders or may complicate a large number of different diseases. Among them chronic renal failure is probably the most common cause of itching. The association between uraemia and pruritus has already been reported more than a century ago. For many years, however, itching has been considered to be too trivial a symptom of uraemia to require careful investigation. It is only recently, after the advent of dialysis has brought control of more severe signs and symptoms of uraemia, that nephrologists and dermatologists have started to dedicate attention to this ‘dermatological non-disease’.
How frequent is pruritus in dialysis patients?

Some 40% of patients suffer from itching at the start of renal replacement therapy while, at least from anamnetic records, 60–90% of patients on regular dialysis complain of pruritus [1]. There are no differences either in frequency or in severity of pruritus between patients treated with haemodialysis or peritoneal dialysis [1]. In about half the cases pruritus is generalized. The back and the arm of dialysis are the preferred sites of localized pruritus. The skin may appear normal or may show lichenification (thickening, with scales caused by scratching), multiple brown nodules covered by crusts and abrasions (prurigo nodularis), or red, violaceous, keratotic papules with a typical central plug. Whenever skin lesions develop as a consequence of pruritus they further worsen itching and scratching leading to a vicious circle. In a number of patients itching may lead to insomnia. In its more severe manifestations it may be so disabling and distressing as to drive its sufferers to contemplate suicide.

What is the pathophysiology of pruritus?

The pathophysiology of dialysis pruritus is still unknown. The problem is rendered even more complex by the emotional conflicts often present in dialysis patients. Mental stress can, in fact, trigger an outburst of pruritus. Moreover, itching is a subjective experience and is therefore difficult to quantitate. A number of different mechanisms have been proposed to explain the origin of uraemic pruritus but none of them is completely convincing. It has been speculated that xerosis (dryness of the skin), which is extremely frequent in dialysis patients, might favour pruritus by modifying cutaneous permeability. However, no relationship has been found between the severity of xerosis and that of pruritus [1,2] and the transpidermal water loss has been shown to be normal in dialysis patients, indicating that uraemic pruritus is not related to abnormalities of cutaneous permeability [3]. Theoretically the accumulation of pruritogenic substances not removed by dialysis might exert its effect on itch centres or receptors.

Among the various possible substances, vitamin A, parathyroid hormone, and histamine could have the potential for inducing itching. There is no convincing evidence, however, that any of these substances is responsible for uraemic pruritus. Plasma levels of vitamin A are increased in dialysis patients but there is no relationship between plasma levels of vitamin A and severity of pruritus; moreover autopic studies demonstrated that the content of vitamin A in various organs was similar or lower in uraemia than in non-uraemic patients (reviewed in [1]). Hyperparathyroidism can stimulate mast cells to release histamine and can favour microprecipitation of calcium and magnesium salts in the skin; moreover pruritus can completely disappear after parathyroidectomy. However, it is a common experience that not all the patients with severe hyperparathyroidism have pruritus. Moreover there is no relationship between the plasma levels of parathormone and dermal cell proliferation, nor is there a difference between pruritic and non-pruritic patients with respect to the mean number of mast cells or the mean levels of parathyroid hormone [1–3]. Finally, parathyroidectomized patients made hypercalcaemic with vitamin D still suffer from pruritus.

Increased plasma levels of histamine are elevated in uraemic patients but the correlation between the levels of histamine and the severity of pruritus is still unclear. On the other hand it is difficult to believe that histamine plays an important pathogenic role, since histamine antagonists are ineffective in uraemic pruritus. The flare reaction to histamine is even smaller in uraemic patients than in normal subjects [2]. Another substance with pruritogenic potential is interleukin-1, which can be released after the contact of plasma with bioincompatible haemodialysis membranes. Interleukin-1 has a proinflammatory effect on the skin and might theoretically contribute to the pathogenesis of itching. As recalled before, however, there is no difference in the frequency and severity of pruritus between patients treated with haemodialysis and those treated with peritoneal dialysis, for whom no problem of biocompatibility can be advocated. As an alternative explanation to that of retention of pruritogenic substances, Ståle-Backdahl [2] hypothesized that uraemic pruritus might be due to an abnormal proliferation of sensory nerve fibres in the setting of uraemic neuropathy. She found nerve fibres and terminal sprouting throughout the epidermal layers of dialysis patients. However, a recent report detected no difference between uraemic and normal subjects in the epidermal distribution of enolase-positive sensory nerve fibres [4]. In summary, there is no evidence that uraemic pruritus can be caused by a single factor. It is more likely that several mechanisms—psychological troubles, biochemical abnormalities, altered local reactivity etc.—may be involved in its pathogenesis, and may have a different relevance in different patients.

How to treat pruritus

Because of the ignorance about its pathogenesis it is not surprising that treatment of uraemic pruritus is quite unsatisfactory. Charcoal, cholestyramine, intravenous lidocaine, magnesium-free dialysis, nicergoline, and phototherapy with ultraviolet B light have been proposed for managing uraemic itching. A meta-analysis of randomized clinical trials [5] concluded that among these treatments ultraviolet B (UVB) phototherapy is the treatment of choice in moderate to severe pruritus. The exposure dose ranged in different studies between 5.7 ml/cm² of Westhouse UVB given three times a week and 480 ml/cm² given twice weekly for 2–4 weeks. Unfortunately the results with UVB phototherapy are transient and some patients may require repeat treatment, with potential severe side-effects in the long term. Recently a reduction of plasma histamine levels and a significant improvement of pruritus have been reported in dialysis patients.
during erythropoietin therapy [6]. These results have not been confirmed by another controlled study [7].

Favourable effects with electrical needle stimulation, ketotifen, which is a mast-cell stabilizer, and topical capsaicin, which would deplete the pruritogenic substance P in peripheral sensory neurons have been reported. These trials have been conducted on very small numbers of patients and need to be confirmed by further studies.

Waiting for more intensive investigations on this orphan symptom we suggest the following approach. First the pruritic patient should be evaluated by a dermatologist to rule out any cause of itching other than uraemia. Then the adequacy of dialysis should be carefully checked. It is a common experience that pruritus is more frequent in underdialysed patients and may improve by increasing the efficacy of dialysis. The calcium-phosphorus product should be kept as low as a possible to avoid microprecipitations that can irritate the skin. Adequate measures should be taken to treat severe hyperparathyroidism. In well-dialysed patients without specific skin disease or severe hyperparathyroidism, we suggest starting with UVB phototherapy. Nicergoline (30 mg q. day per os) may be offered to the few non-responders. Electrical needle stimulation, ketotifen (1–2 mg b.day) or topical capsaicin can be considered as possible alternatives. Last but not least the nephrologist should be aware that many itching states have a psychological background. A number of these cases may be improved or even cured simply by listening to the problems of the patient in warm and cordial conversations.

References

Identifying the high-risk dialysis patient: what are the benefits?

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Introduction

Contemporary patients receiving renal replacement therapy (RRT) in Europe bear little resemblance to those given treatment up to the mid 1980s. As recently as 1984 a study from the UK [1] showed that some nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from nephrologists considered blindness, dementia, and inability to speak English as reasons for exclusion from