INVESTIGATIVE REPORT

Use of Systemic Treatment in Patients with Chronic Pruritus: A Survey of Dermatologists in the Netherlands

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Treatment of chronic pruritus can be a challenge for clinicians. Several systemic treatments have been suggested to reduce itch, such as gabapentinoids and antidepressants. The aim of this study was to assess the current practice of dermatologists regarding systemic treatment in patients with chronic pruritus, and to identify possible barriers in the prescription of these treatments. An online survey was sent to all dermatologists and dermatology residents in the Netherlands between July 2017 and April 2018. A total of 193 physicians completed the questionnaire (response rate 27.0%). Overall, 61.7% prescribed gabapentinoids or antidepressants in patients with chronic pruritus. Amitriptyline was prescribed most frequently, followed by gabapentin, doxepin and mirtazapine. Reasons not to prescribe systemic treatment included lack of knowledge or experience, risk of side-effects, and lack of available evidence. As only a minority of respondents felt comfortable prescribing these drugs, more education on effective and safe dosing is needed.

Key words: pruritus; therapeutics; gabapentin; antidepressive agents; survey.

Accepted Dec 6, 2018; E-published Dec 6, 2018

Acta Derm Venereol 2019; 99: 304–308.

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SIGNIFICANCE

This study analysed the prescription of systemic treatment by dermatologists in patients with chronic itch. Overall, 6 out of 10 dermatologists prescribed antidepressants or gabapentinoids, of which, antidepressants were prescribed most frequently. Reasons not to prescribe systemic treatment included lack of knowledge or experience, risk of side-effects, and lack of available evidence. Only a minority of the clinicians surveyed felt comfortable prescribing these drugs; therefore, we recommend more education on effective and safe dosing.

Itch is one of the most common symptoms presented in daily dermatological practice, with an estimated point prevalence of 36.2% (1–3). Chronic pruritus (CP) (itch present for a minimum of 6 weeks) can be caused by several dermatological, systemic, neurological and psychiatric disorders (2, 4). CP is associated with a reduced quality of life, including impact on mood, concentration and sleep, and a higher risk of anxiety and depression (5–8).

Several systemic treatment options have been suggested for patients with CP (2, 9–11). For example gabapentinoids, such as gabapentin and pregabalin, were used in patients with uremic pruritus and neurogenic itch (12–20). In addition, treatment with oral antidepressants, such as mirtazapine, paroxetine and sertraline, have been recommended in patients with pruritus unresponsive to conventional treatment options, and particularly in patients with uraemic pruritus, cholestatic pruritus or paraneoplastic pruritus (21–28). Other systemic treatment options include opioid receptor agonists and antagonists, thalidomide and neurokinin 1 receptor (NKR1) antagonists (29–36).

Due to its heterogeneity and difficult to establish underlying origin, treatment of CP remains a challenge for clinicians (37, 38). If systemic treatment is initiated, side-effects can complicate therapeutic attempts, especially in elderly patients. In addition, dermatologists might not feel comfortable prescribing psychotropic medication (39). Data on the use of systemic treatments for CP by clinicians in daily practice is currently scarce.

The aim of this study was to provide more insight into the current practice of dermatologists regarding systemic treatment in patients with CP, including identification of the treatments used, clinicians' experiences on reducing itch after initiation of systemic treatment, and possible barriers to prescription of systemic treatment.

METHODS

An anonymous web-based questionnaire was sent by e-mail to all members of the Dutch Society of Dermatology and Venereology (NVDV) between July 2017 and April 2018. It was first piloted to dermatologists ($n = 3$) and dermatology residents ($n = 6$) in June 2017 at the Radboud University Medical Center, Nijmegen, the Netherlands, resulting in the adaptation of a few questions and instructions to avoid ambiguity. The final questionnaire consisted of 19 questions, including multiple-choice questions, 5-point Likert scale questions and open-ended questions. Participants were asked about demographic and professional data, prevalence of CP in their clinical practice, use of antiepileptics and antidepressants in treatment of CP, their level of comfort in prescribing these pharmaceuticals and other systemic treatment options used in treatment of CP. In this survey, CP was defined as itch present for a minimum of 6 weeks due to both dermatological and non-dermatological conditions. Study data were collected and managed

doi: 10.2340/00015555-3101
Acta Derm Venereol 2019; 99: 304–308

Table I. Demographics of survey respondents ($n = 193$)

Characteristics of respondents	
Sex, *n* (%)	
Male	62 (32.1)
Female	131 (67.9)
Age, years ($n = 190$) mean ± SD	42.7 ± 10.6
Profession, *n* (%)	
Dermatologist	155 (80.3)
Dermatology resident	38 (19.7)
Practice setting[a], *n* (%)	
Academic hospital	60 (31.1)
General hospital	117 (60.6)
Private practice	31 (16.1)
Other	4 (2.1)
Years of clinical experience, *n* (%)	
0–10 years	96 (49.7)
10–20 years	50 (25.9)
> 20 years	47 (24.4)

[a]Total number of respondents does not equal sum of respondents reporting different practice settings because more than one setting can be reported by the same respondent.
SD: standard deviation.

by Qualtrics web-based survey software (Provo, UT, USA). The entire survey is available in Table SI[1].

Data of respondents were displayed as means and standard deviations (SD) for continuous variables, and numbers and percentages for categorical variables (*n* (%)). Age, sex, profession and practice setting of the respondent population were compared with the target population to test for selection bias. Subgroup analyses were conducted to compare the influence of physician subgroup, years of clinical experience and practice setting on the prescription of systemic treatments using independent χ^2 tests. $p < 0.05$ was considered statistically significant. All statistical analyses were performed with SPSS, version 22.0 (IBM SPSS Inc, Chicago, USA).

RESULTS

A total of 193 members responded (response rate 27.0%), including 155 (80.3%) dermatologists and 38 (19.7%) dermatology residents (**Table I**). The mean ± SD age of all respondents (67.9% women) was 42.7 ± 0.6 years. Most respondents practiced in a general hospital (60.6%) or academic hospital (31.1%). A comparison of sex, age, profession and practice setting between the respondent population and target population showed no significant differences (data available on request).

Prevalence of chronic pruritus

Respondents were asked to estimate the number of patients seen with CP that could not be resolved by treatment of an underlying cause or by conventional treatment options (e.g. topical treatments or oral antihistamines), and therefore had a possible indication for systemic treatment. Most respondents estimated that they saw at least one patient in the described population per week (33.2%) or per month (33.7%), followed by one patient per 3 months (13%) or even one patient per day (9.8%) (**Table II**).

[1]https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3101

Use of gabapentin and pregabalin

Overall, 74 (38.3%) respondents prescribed gabapentinoids for patients with CP (Table II), of whom 47 (64.4%) prescribed gabapentin, 10 (13.7%) prescribed pregabalin and 16 (21.9%) prescribed both. When these respondents were asked about the efficacy of these treatments on reducing itch using a 5-point Likert scale (ranging from very poor to very good), the majority reported a fair (gabapentin 61.9%; pregabalin 66.7%) or good (gabapentin 25.4%; pregabalin 22.2%) treatment effect (**Table III**). Significantly more respondents who are currently working in an academic hospital (66.0%; $p = 0.000$) prescribed gabapentin or pregabalin compared with respondents working in general hospitals (26.7%) or private practices (19.0%) (Table SII[1]). In addition, significant differences were found according to profession (dermatologist 32.9%; dermatology resident 60.5%; $p = 0.002$) and clinical experience (0–10 years 51.0%; 10–20 years 24.0%; > 20 years 27.7%; $p = 0.001$). When respondents not prescribing gabapentin or pregabalin ($n = 119$; 61.7%) were asked to explain why they did not prescribe these pharmaceuticals, the majority stated they did not have

Table II. Prevalence of chronic pruritus in daily clinical practice, prescription of antiepileptic treatment in patients with chronic pruritus (CP) and prescription of antidepressants in patients with CP

Indication of patients seen in daily clinical practice with CP and an indication for systemic treatment estimated by survey respondents (n=193), n (%)	
Every day	19 (9.8)
Every week	64 (33.2)
Every month	65 (33.7)
Every 3 months	25 (13.0)
Every 6 months	11 (5.7)
Every year	6 (3.1)
Less than once per year	3 (1.6)
Prescription of antiepileptic treatment in patients with CP, n (%)	
Prescription of antiepileptic treatment for CP ($n = 193$)	
Yes	74 (38.3)
No	119 (61.7)
Specification of antiepileptic treatment prescribed for CP[a] ($n = 74$)	
Gabapentin	63 (85.1)
Pregabalin	26 (35.1)
Reasons not to prescribe antiepileptic treatment for patients with CP[a] ($n = 119$)	
Not enough knowledge or experience	103 (86.6)
Side-effects	16 (13.4)
Not enough evidence	11 (9.2)
Interactions	1 (0.8)
Other	12 (10.1)
Prescription of antidepressants in patients with CP, n (%)	
Prescription of antidepressants for CP ($n = 192$)	
Yes	101 (52.6)
No	91 (47.4)
Specification of antidepressants prescribed for CP[a] ($n = 101$)	
Amitriptyline	82 (81.2)
Doxepin	30 (29.7)
Mirtazapine	13 (12.9)
Paroxetine	12 (11.9)
Nortriptyline	7 (6.9)
Fluoxetine	2 (2.0)
Sertraline	2 (2.0)
Reasons not to prescribe antidepressants for patients with CP[a] ($n = 91$)	
Not enough knowledge or experience	80 (87.9)
Side-effects	15 (16.5)
Not enough evidence	11 (12.1)
Interactions	1 (1.1)
Other	5 (5.5)

[a]Total number of respondents does not equal sum of patients reporting different outcomes because more than one can be reported by the same respondent.

Table III. Respondent experiences on reducing itch after initiation of antiepileptic medication ($n=74$) or antidepressants ($n=101$) using a 5-point Likert scale

	Very poor *n* (%)	Poor *n* (%)	Fair *n* (%)	Good *n* (%)	Very good *n* (%)
Gabapentin ($n=63$)	1 (1.6)	4 (6.3)	39 (61.9)	16 (25.4)	3 (4.8)
Pregabalin ($n=26$)	0	3 (11.5)	17 (65.4)	6 (23.1)	0
Amitriptyline ($n=82$)	0	5 (6.1)	54 (65.9)	23 (28.0)	0
Doxepin ($n=30$)	0	2 (6.7)	14 (46.7)	14 (46.7)	0
Mirtazapine ($n=13$)	0	0	11 (84.6)	1 (7.7)	1 (7.7)
Paroxetine ($n=12$)	1 (8.3)	0	9 (75.0)	2 (16.7)	0
Nortriptyline ($n=7$)	0	0	4 (57.1)	3 (42.9)	0
Fluoxetine ($n=2$)	0	0	1 (50.0)	1 (50.0)	0
Sertraline ($n=2$)	0	0	2 (100.0)	0	0

enough knowledge or experience (86.5%), followed by risk of side-effects of gabapentinoids (13.4%) and lack of available evidence on efficacy of antiepileptic treatment (9.2%) (Table II). Two respondents stated that they had not heard of the option of gabapentin or pregabalin treatment for CP.

Use of antidepressants

Over half of those surveyed (52.6%) prescribed oral antidepressants for treatment of CP (Table II). The majority of these respondents prescribed amitriptyline (81.2%), followed by doxepin (29.7%), mirtazapine (12.9%), paroxetine (11.9%) and nortriptyline (6.9%). Only 2 respondents prescribed fluoxetine (2.0%) or sertraline (2.0%). The treatment effect of these drugs was mostly rated as 'fair' or 'good' (Table III). One respondent even reported a 'very good' treatment effect after initiation of mirtazapine. No significant differences in prescription of antidepressants were found with respect to profession, years of clinical experience or practice setting (Table SII[1]). Respondents not prescribing antidepressants ($n=91$; 47.4%) stated they had not enough knowledge or experience (87.9%); or were worried about side-effects (16.5%) and lack of available evidence (12.1%) (Table II).

Being comfortable about prescribing antiepileptic and antidepressant drugs

When participants were asked if they were comfortable about prescribing gabapentinoids, the majority disagreed (32.3%), or strongly disagreed (20.3%) (**Table IV**). When these outcomes were specified for respondents prescribing gabapentin or pregabalin, more respondents reported feeling comfortable (30.1% vs. 11.8%; $p=0.000$). The same was true for prescription of antidepressants, as the majority of respondents also disagreed about feeling comfortable prescribing these drugs (34.2%), and more respondents felt comfortable if they were actually prescribing these treatments (27.7% vs. 11.0%; $p=0.000$).

Other treatment options

When asked about other treatment options used by respondents in daily clinical practice for the treatment of CP, the majority of respondents reported oral immunosuppressants, such as methotrexate or cyclosporine A, and opioid antagonists, such as naltrexone. Other suggestions were haloperidol, ondansetron and thalidomide.

DISCUSSION

This survey was conducted to investigate the current practice of dermatologists and dermatology residents in the Netherlands regarding systemic treatment in patients with CP. More than 40% of respondents reported having seen patients with CP and a possible indication for systemic treatment at least once per day or once per week, and another 30% reported seeing such patients at least once every month. As this is even more than the estimated point prevalence of CP described earlier in a cross-sectional study in dermatological practice (1), a large group of patients demands an effective and safe treatment for their symptoms.

Table IV. Respondents feeling comfortable prescribing antiepileptic treatment and antidepressants for the treatment of itch

	Total respondents ($n=192$) *n* (%)	Prescribing antiepileptic treatment ($n=73$) *n* (%)	Not prescribing antiepileptic treatment ($n=119$) *n* (%)	*p*-value
'I feel comfortable prescribing antiepileptic treatment'				0.000
Strongly disagree	39 (20.3)	2 (2.7)	37 (31.1)	
Disagree	62 (32.3)	12 (16.4)	50 (42.0)	
Neither agree or disagree	44 (22.8)	35 (47.9)	9 (7.6)	
Agree	36 (18.7)	22 (30.1)	14 (11.8)	
Strongly agree	11 (5.7)	2 (2.7)	9 (7.6)	
		Prescribing antidepressants ($n=101$) *n* (%)	Not prescribing antidepressants ($n=91$) *n* (%)	
'I feel comfortable prescribing antidepressants'				0.000
Strongly disagree	24 (12.4)	2 (2.0)	22 (24.2)	
Disagree	66 (34.2)	20 (19.8)	46 (50.5)	
Neither agree or disagree	56 (29.0)	48 (47.5)	8 (8.8)	
Agree	38 (19.7)	28 (27.7)	10 (11.0)	
Strongly agree	8 (4.1)	3 (3.0)	5 (5.5)	

In our study, more than half of the physicians surveyed (52.6%) have prescribed antidepressants in patients with CP. The most commonly prescribed antidepressant was amitriptyline (81.2%). However, evidence for the use of amitriptyline in the treatment of CP is limited, as it was described in only one observational study, 2 case series and 3 case reports, mainly describing patients with pruritus of neuropathic origin (e.g. brachioradial pruritus or notalgia paraesthetica) (40–45). The other frequently prescribed antidepressants, doxepin (29.7%), mirtazapine (12.9%) and paroxetine (11.9%), have been described more frequently, mostly for paraneoplastic pruritus, uremic pruritus or pruritus of unknown origin (21, 23, 24, 28, 46–50), and were recommended in guidelines for various forms of CP not responsive to conventional treatment options (2, 9, 51). This discrepancy could be explained as amitriptyline is an established pharmacological intervention for neuropathic pain (52), and is therefore well known by most dermatologists.

According to the respondents in our survey, gabapentinoids are prescribed less frequently in daily practice compared with antidepressants (38.3% vs. 52.6%). Of these 2 treatments, gabapentin is prescribed more often compared with pregabalin (65.0% vs. 35.0%), probably as pregabalin is a relatively new drug with fewer studies examining its use in patients with CP (10). In addition, evidence comparing the efficacy of gabapentin and pregabalin is limited, with only one open-label trial in haemodialysis patients with neuropathic pruritus ($n = 40$), showing no significant difference between the 2 pharmaceuticals (53).

Almost all respondents not prescribing antiepileptics or antidepressants (86.5% and 87.9%, respectively), stated they had limited knowledge or experience to initiate these treatments. In addition, 2 respondents stated that they never heard of the option of gabapentin or pregabalin treatment in patients with CP. Lack of experience and knowledge was also shown by the low rates of respondents feeling comfortable prescribing these drugs. For example, more than half of respondents prescribed antidepressants, with only 23.8% feeling comfortable or very comfortable prescribing them. These results are similar to a previous survey evaluating the use of psychotropic treatment among dermatologists ($n = 59$), showing that only a few dermatologists felt comfortable (11%) or very comfortable (3%) prescribing antidepressants for psychocutaneous disorders (39). Interestingly, in the same population far more dermatologists felt comfortable (66%) or very comfortable (18%) starting treatment for neuropathic pain, including gabapentin and pregabalin. It is important to acknowledge dermatologists' lack of knowledge and experience on prescription of these drugs, especially as not all patients can be seen in specialized centres due to the high prevalence of this symptom. Use of guidelines, education on effective and safe dosing, and close cooperation with specialized centres can be helpful to improve care of CP.

In a recent survey conducted in Germany, patients with CP reported finding a clear diagnosis and therapy, being free of itch and having confidence in the therapy as their most important treatment goals (54). However, effective treatment of CP remains a challenge for clinicians, often using gabapentinoids and antidepressants as a last resort (37, 38). As these pharmaceuticals might have substantial side-effects, especially in geriatric patients or patients with multiple comorbidities or concomitant medications, and are not registered for treatment of CP, there is still an unmet need for an effective and safe treatment (10, 11).

A limitation of our survey is the response rate of approximately 30%, and therefore a risk of selection bias. However, no significant differences in age, sex, profession and practice setting were found between our response population and the target population.

In conclusion, over half of respondents of our survey prescribed antidepressants for treatment of pruritus. Even though evidence is scarce, amitriptyline was prescribed most often, followed by mirtazapine, doxepin and paroxetine. Compared with antidepressants, gabapentin and pregabalin were prescribed less frequently. A minority of respondents felt comfortable prescribing these treatments, and a lack of knowledge and experience was considered the main reason not to prescribe antiepileptic of antidepressant treatment. Therefore, we recommend more education on effective and safe dosing.

The authors have no conflicts of interest to declare.

REFERENCES

1. Kopyciok MER, Ständer HF, Osada N, Steinke S, Ständer S. Prevalence and characteristics of pruritus: a one-week cross-sectional study in a German dermatology practice. Acta Derm Venereol 2016; 96: 50–55.
2. Weisshaar E, Szepietowski JC, Darsow U, Misery L, Wallengren J, Mettang T, et al. European guideline on chronic pruritus. Acta Derm Venereol 2012; 92: 563–581.
3. Yosipovitch G, Bernhard JD. Clinical practice. Chronic pruritus. N Engl J Med 2013; 368: 1625–1634.
4. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. Acta Derm Venereol 2007; 87: 291–294.
5. Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M. A questionnaire for the assessment of pruritus: validation in uremic patients. Acta Derm Venereol 2001; 81: 108–111.
6. Grundmann S, Ständer S. Chronic pruritus: clinics and treatment. Ann Dermatol 2011; 23: 1–11.
7. Dalgard F, Lien L, Dalen I. Itch in the community: associations with psychosocial factors among adults. J Eur Acad Dermatol Venereol 2007; 21: 1215–1219.
8. Halvorsen JA, Dalgard F, Thoresen M, Thoresen M, Bjertness E, Lien L. Itch and mental distress: a cross-sectional study among late adolescents. Acta Derm Venereol 2009; 89: 39–44.
9. Millington GWM, Collins A, Lovell CR, Leslie TA, Yong ASW, Morgan JD, et al. British Association of Dermatologists' guidelines for the investigation and management of generalized pruritus in adults without an underlying dermatosis, 2018. Br J Dermatol 2018; 178: 34–60.

10. Matsuda KM, Sharma D, Schonfeld AR, Kwatra SG. Gabapentin and pregabalin for the treatment of chronic pruritus. J Am Acad Dermatol 2016; 75: 619–625 e616.
11. Kouwenhoven TA, van de Kerkhof PCM, Kamsteeg M. Use of oral antidepressants in patients with chronic pruritus: a systematic review. J Am Acad Dermatol 2017; 77: 1068–1073 e1067.
12. Gunal AI, Ozalp G, Yoldas TK, Gunal SY, Kirciman E, Celiker H. Gabapentin therapy for pruritus in haemodialysis patients: a randomized, placebo-controlled, double-blind trial. Nephrol Dial Transplant 2004; 19: 3137–3139.
13. Naini AE, Harandi AA, Khanbabapour S, Shahidi S, Seirafiyan S, Mohseni M. Gabapentin: a promising drug for the treatment of uremic pruritus. Saudi J Kidney Dis Transpl 2007; 18: 378–381.
14. Manenti L, Vaglio A, Costantino E, Danisi D, Oliva B, Pini S, et al. Gabapentin in the treatment of uremic itch: an index case and a pilot evaluation. J Nephrol 2005; 18: 86–91.
15. Razeghi E, Eskandari D, Ganji MR, Meysamie AP, Togha M, Khashayar P. Gabapentin and uremic pruritus in hemodialysis patients. Ren Fail 2009; 31: 85–90.
16. Winhoven SM, Coulson IH, Bottomley WW. Brachioradial pruritus: response to treatment with gabapentin. Br J Dermatol 2004; 150: 786–787.
17. Yue J, Jiao S, Xiao Y, Ren W, Zhao T, Meng J. Comparison of pregabalin with ondansetron in treatment of uraemic pruritus in dialysis patients: a prospective, randomized, double-blind study. Int Urol Nephrol 2015; 47: 161–167.
18. Maciel AA, Cunha PR, Laraia IO, Trevisan F. Efficacy of gabapentin in the improvement of pruritus and quality of life of patients with notalgia paresthetica. An Bras Dermatol 2014; 89: 570–575.
19. Aperis G, Paliouras C, Zervos A, Arvanitis A, Alivanis P. The use of pregabalin in the treatment of uraemic pruritus in haemodialysis patients. J Ren Care 2010; 36: 180–185.
20. Shavit L, Grenader T, Lifschitz M, Slotki I. Use of pregabalin in the management of chronic uremic pruritus. J Pain Symptom Manage 2013; 45: 776–781.
21. Zylicz Z, Krajnik M, Sorge AA, Costantini M. Paroxetine in the treatment of severe non-dermatological pruritus: a randomized, controlled trial. J Pain Symptom Manage 2003; 26: 1105–1112.
22. Zylicz Z, Smits C, Krajnik M. Paroxetine for pruritus in advanced cancer. J Pain Symptom Manage 1998; 16: 121–124.
23. Diehn F, Tefferi A. Pruritus in polycythaemia vera: prevalence, laboratory correlates and management. Br J Haematol 2001; 115: 619–621.
24. Ständer S, Bockenholt B, Schurmeyer-Horst F, Weishaupt C, Heuft G, Luger TA, et al. Treatment of chronic pruritus with the selective serotonin re-uptake inhibitors paroxetine and fluvoxamine: results of an open-labelled, two-arm proof-of-concept study. Acta Derm Venereol 2009; 89: 45–51.
25. Mayo MJ, Handem I, Saldana S, Jacobe H, Getachew Y, Rush AJ. Sertraline as a first-line treatment for cholestatic pruritus. Hepatology 2007; 45: 666–674.
26. Shakiba M, Sanadgol H, Azmoude HR, Mashhadi MA, Sharifi H. Effect of sertraline on uremic pruritus improvement in ESRD patients. Int J Nephrol 2012; 2012: 363901.
27. Thebaut A, Habes D, Gottrand F, Rivet C, Cohen J, Debray D, et al. Sertraline as an additional treatment for cholestatic pruritus in children. J Pediatr Gastroenterol Nutr 2017; 64: 431–435.
28. Davis MP, Frandsen JL, Walsh D, Andresen S, Taylor S. Mirtazapine for pruritus. J Pain Symptom Manage 2003; 25: 288–291.
29. Winkelmann RK, Connolly SM, Doyle JA, Padilha-Goncalves A. Thalidomide treatment of prurigo nodularis. Acta Derm Venereol 1984; 64: 412–417.
30. Ferrandiz C, Carrascosa JM, Just M, Bielsa I, Ribera M. Sequential combined therapy with thalidomide and narrow-band (TL01) UVB in the treatment of prurigo nodularis. Dermatology 1997; 195: 359–361.
31. Bergasa NV, Alling DW, Talbot TL, Swain MG, Yurdaydin C, Turner ML, et al. Effects of naloxone infusions in patients with the pruritus of cholestasis. A double-blind, randomized, controlled trial. Ann Intern Med 1995; 123: 161–167.
32. Wolfhagen FH, Sternieri E, Hop WC, Vitale G, Bertolotti M, Van Buuren HR. Oral naltrexone treatment for cholestatic pruritus: a double-blind, placebo-controlled study. Gastroenterology 1997; 113: 1264–1269.
33. Phan NQ, Bernhard JD, Luger TA, Ständer S. Antipruritic treatment with systemic mu-opioid receptor antagonists: a review. J Am Acad Dermatol 2010; 63: 680–688.
34. Wikstrom B, Gellert R, Ladefoged SD, Danda Y, Akai M, Ide K, et al. kappa-opioid system in uremic pruritus: Multicenter, randomized, double-blind, placebo-controlled clinical studies. J Am Soc Nephrol 2005; 16: 3742–3747.
35. Ständer S, Siepmann D, Herrgott I, Sunderkotter C, Luger TA. Targeting the neurokinin receptor 1 with aprepitant: a novel antipruritic strategy. PLoS One 2010; 5: e10968.
36. Yosipovitch G, Ständer S, Kerby MB, Larrick JW, Perlman AJ, Schnipper EF, et al. Serlopitant for the treatment of chronic pruritus: results of a randomized, multicenter, placebo-controlled phase 2 clinical trial. J Am Acad Dermatol 2018; 78: 882–891 e810.
37. Pereira MP, Ständer S. Chronic pruritus: current and emerging treatment options. Drugs 2017; 77: 999–1007.
38. Ständer S, Pogatzki-Zahn E, Stumpf A, Fritz F, Pfleiderer B, Ritzkat A, et al. Facing the challenges of chronic pruritus: a report from a multi-disciplinary medical itch centre in Germany. Acta Derm Venereol 2015; 95: 266–271.
39. Gee SN, Zakhary L, Keuthen N, Kroshinsky D, Kimball AB. A survey assessment of the recognition and treatment of psychocutaneous disorders in the outpatient dermatology setting: how prepared are we? J Am Acad Dermatol 2013; 68: 47–52.
40. Barry R, Rogers S. Brachioradial pruritus – an enigmatic entity. Clin Exp Dermatol 2004; 29: 637–638.
41. Yew YW, Tey HL. Itch in familial lichen amyloidosis: effective treatment with amitriptyline in two cases. Dermatol Ther 2014; 27: 12–15.
42. Yong A, Chong WS, Tey HL. Effective treatment of uremic pruritus and acquired perforating dermatosis with amitriptyline. Australas J Dermatol 2014; 55: e54–57.
43. Crevits L. Brachioradial pruritus – a peculiar neuropathic disorder. Clin Neurol Neurosurg 2006; 108: 803–805.
44. Yeo B, Tey HL. Effective treatment of notalgia paresthetica with amitriptyline. J Dermatol 2013; 40: 505–506.
45. Ganguly S, Krishna CV, Parmar NV, Kuruvila S, Phansalkar DS. Unilateral pruritus following stroke. Indian J Dermatol Venereol Leprol 2015; 81: 186–188.
46. Sheen MJ, Ho ST, Lee CH, Tsung YC, Chang FL, Huang ST. Prophylactic mirtazapine reduces intrathecal morphine-induced pruritus. Br J Anaesth 2008; 101: 711–715.
47. Hundley JL, Yosipovitch G. Mirtazapine for reducing nocturnal itch in patients with chronic pruritus: a pilot study. J Am Acad Dermatol 2004; 50: 889–891.
48. Pour-Reza-Gholi F, Nasrollahi A, Firouzan A, Nasli Esfahani E, Farrokhi F. Low-dose doxepin for treatment of pruritus in patients on hemodialysis. Iran J Kidney Dis 2007; 1: 34–37.
49. Shohrati M, Davoudi SM, Keshavarz S, Sadr B, Tajik A. Cetirizine, doxepine, and hydroxyzine in the treatment of pruritus due to sulfur mustard: a randomized clinical trial. Cutan Ocul Toxicol 2007; 26: 249–255.
50. Foroutan N, Etminan A, Nikvarz N, Shojai Shahrokh Abadi M. Comparison of pregabalin with doxepin in the management of uremic pruritus: a randomized single blind clinical trial. Hemodial Int 2017; 21: 63–71.
51. Ständer S, Zeidler C, Augustin M, Bayer G, Kremer AE, Legat FJ, et al. S2k Guidelines for the diagnosis and treatment of chronic pruritus – update – short version. J Dtsch Dermatol Ges 2017; 15: 860–872.
52. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain in adults. Cochrane Database Syst Rev 2015: CD008242.
53. Solak Y, Biyik Z, Atalay H, Gaipov A, Guney F, Turk S, et al. Pregabalin versus gabapentin in the treatment of neuropathic pruritus in maintenance haemodialysis patients: a prospective, crossover study. Nephrology (Carlton) 2012; 17: 710–717.
54. Steinke S, Bruland P, Blome C, Osada N, Dugas M, Fritz F, et al. Chronic pruritus: evaluation of patient needs and treatment goals with a special regard to differences according to pruritus classification and sex. Br J Dermatol 2017; 176: 363–370.