mitigate symptomatic rashes. Patients may be switched to another antimalarial; desensitization or dose titration may be attempted if hydroxychloroquine is the best/only treatment option.[5] Patients with adverse events, including pruritus (526; 4.7%) and urticaria (419; 4.5%), may also benefit from dose escalation regimens.

This study is subject to several limitations. FAERS data are self-reported by physicians, pharmaceutical companies, and patients, without corroboration. Some case information, dosing/cumulative dosing, and hydroxychloroquine prescribing by year were not available. Non-FDA indications for hydroxychloroquine (mixed connective tissue disease, antiphospholipid syndrome) were included in the data set.

This study substantiates previous studies showing that drug rashes were the most common dermatologic adverse reaction with hydroxychloroquine. We also highlight some of the less frequent and more serious adverse reactions including Stevens-Johnson syndrome/toxic epidermal necrolysis, skin necrosis, and vasculitis.[6]

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Intranasal butorphanol rescue therapy for the treatment of intractable pruritus: A case series from the Johns Hopkins Itch Clinic

To the Editor: Chronic itch that is refractory to conventional therapy is a debilitating symptom that can be difficult to manage clinically. With limited United States Food and Drug Administration-approved therapies specifically targeting itch, there is a clinical need for rapid-acting agents that can disrupt the itch-scratch cycle for patients with refractory chronic pruritus.

Although the mechanism of pruritus is poorly understood, recent breakthroughs highlight a key role for the opioid axis where μ-opioid receptor agonism is thought to potentiate itch, while κ-opioid receptor agonism may reduce itch.[1,2] A recent study saw the rapid reversal of pruritus with naloxone infusion, a μ-opioid antagonist, while other reports have demonstrated significant promise for butorphanol, a commercially available μ-opioid antagonist and κ-opioid agonist, as a salvage therapy providing rapid relief for chronic itch that is refractory to standard first-line therapies.[1,2]

Most reports to date however describe the effectiveness of butorphanol administration for morphine-induced pruritus, because analgesic opioid agents often produce itch as an adverse effect.[2,3] As such, few studies have described the clinical implementation of intranasal butorphanol in treating intractable pruritus associated with a variety of etiologies. We investigated the efficacy of intranasal butorphanol as a rescue therapy for chronic, refractory pruritus.

We report a series of 16 patients who were treated with a butorphanol, 10 mg/mL inhaler as needed, up to every 4 hours for intractable pruritus from June 2017 to July 2019 at the Johns Hopkins Itch Clinic. We conducted a retrospective medical record review and collected data regarding patient characteristics, diagnosis, dose and duration of previously tried therapies, adverse effects, compliance, comorbidities, and improvement in pruritic symptoms using patient- reported outcomes, the worst itch numerical rating scale (WI-NRS), and quality of life survey measures, which were analyzed using paired *t* tests.

Table I. Patient characteristics

Variable*	All patients	Experienced improvement	Unknown or no improvement
Patients	16	13 (81)	3 (19)
Sex			
Female	12 (75)	10 (83)	2 (17)
Male	4 (25)	3 (75)	1 (25)
Race			
White	7 (44)	6 (86)	1 (14)
Black/African American	6 (38)	5 (83)	1 (17)
Other	1 (6)	1 (100)	0
Asian	2 (13)	1 (50)	1 (50)
Marital status			
Single	7 (44)	5 (71)	2 (29)
Married	8 (50)	7 (88)	1 (12)
Widowed	1 (6)	1 (100)	0
Occupation			
Unemployed	9 (56)	5 (56)	4 (44)
Diagnosis			
Concomitant atopic dermatitis	7 (31)	5 (71)	2 (29)
Concomitant prurigo nodularis	3 (13)	2 (67)	1 (33)
Age, y	60.63 ± 2.96	61.45 ± 4.26	58.8 ± 2.01

*Data are presented as number (%) or mean ± SD.

Table II. Summary of patients with chronic refractory pruritus treated with butorphanol

Patient	Age, y	Diagnosis	Failed therapies	Butorphanol adverse effects	Improvement in symptoms, time to follow up
1	59	Aquagenic pruritus	Desloratadine (60 mg/d) Naltrexone (50 mg) Phototherapy Hydroxyzine (20 mg/d) Gabapentin	Yes, insomnia	Yes, 6 wk
2	82	Chronic pruritus of unknown origin	Triamcinolone acetonide BID Diphenhydramine Ivermectin Prednisone (10 mg) Phototherapy	No	Yes, 7 wk
3	55	Atopic dermatitis	Gabapentin Dupilumab Naloxone Triamcinolone Aprepitant	No	Yes, 4 wk
4	50	Brachioradial pruritus	Triamcinolone cream Clobetasol Pregabalin Aprepitant Phototherapy Paroxetine	No	Yes, 8 wk
5	79	Chronic idiopathic urticaria	Antihistamines Clobetasol Kenalog (60 mg IM) Omalizumab Triamcinolone Menthol Phototherapy Sulfasalazine	Yes, lightheadedness, sleepiness	Yes, 6 wk

Continued

Table II. Cont'd

Patient	Age, y	Diagnosis	Failed therapies	Butorphanol adverse effects	Improvement in symptoms, time to follow up
6	51	Atopic dermatitis	Cyclosporine Methotrexate Mycophenolic acid (1 g/d) Triamcinolone injection (80 mg IM) Triamcinolone Fluocinonide Clindamycin (300 mg) Omalizumab (300 mg monthly) Prednisone Phototherapy Azathioprine Naltrexone Aprepitant Hydroxyzine	No	Yes, 7 wk
7	40	Intrinsic (allergic) eczema	Dupilumab Phototherapy Antihistamines Mirtazapine Gabapentin Paroxetine Methoxsalen (10 mg)	No	Yes, 5 wk
8	61	PD1-inhibitor associated pruritus	Triamcinolone 0.1% ointment Tacrolimus Gabapentin (100 mg qhs) Doxycycline (200 mg/d) Phototherapy Fexofenadine	No	Yes, 4 wk
9	51	Neuropathic pruritus	Doxepin Mirtazapine Hydroxyzine Gabapentin Triamcinolone Diphenhydramine Duloxetine Diclofenac gel Lidocaine topical Capsaicin patch	No	Yes, 4 wk
10	81	Prurigo nodularis	Pregabalin (150 mg/d) Flurandrenolide Cyclosporine Mycophenolic acid Naltrexone Pregabalin Phototherapy Methotrexate	No	Yes, 8 wk
11	67	Chronic pruritus in setting of primary sclerosing cholangitis with lichen amyloidosis	Phototherapy Naltrexone (25 mg) Fluocinonide Ammonium nitrate Dronabinol (5 mg) Cholestyramine	Yes, sleepiness	Yes, 6 wk

Continued

Table II. Cont'd

Patient	Age, y	Diagnosis	Failed therapies	Butorphanol adverse effects	Improvement in symptoms, time to follow up
12	62	Pruritus possibly of cervicogenic/neuropathic etiology	Mirtazapine Gabapentin (2700 mg/d) Antihistamines Lidocaine/ketamine/amitriptyline topical Doxepin Naltrexone (25 mg)	No	No
13	61	Prurigo nodularis	Pregabalin Mirtazapine Aprepitant Ketamine/amitriptyline/lidocaine lotion Diphenhydramine Phototherapy Menthol 2% with Lubriderm* Triamcinolone Hydroxyzine	No	Unknown
14	63	Atopic dermatitis	Mycophenolic acid 500/250 mg Triamcinolone Phototherapy Tacrolimus	No	Unknown
15	53	Prurigo nodularis	Gabapentin Topical steroids Phototherapy Antihistamines Fluocinonide	No	Yes, 10 wk
16	55	Trigeminal trophic syndrome	Amitriptyline (100 mg/d) Clonazepam (4 mg/d) Gabapentin (900 mg/d) Ketamine/amitriptyline/lidocaine/Pramoxine Oxycodone (30 mg/d) Cyclobenzaprine (20 mg/d) Lamotrigine (150 mg/d) Celecoxib (200 mg) Pimecrolimus 1% cream	No	Yes, 10 wk

BID, Twice daily; *IM*, intramuscular; *PD-1*, programmed cell death protein 1; *qhs*, every evening at bedtime.
*Johnson & Johnson Consumer Inc, New Brunswick, NJ.

A summary of the patient demographics is provided in Table I. The mean WI-NRS score before butorphanol initiation was 9.78 ± 0.15. Thirteen patients (81%) reported improvement in pruritus after initiation of butorphanol, with a mean response time of 6.53 ± 1.99 weeks. Improvement was determined by WI-NRS scores or patients' reports of improvement, or both. Of the patients reporting improvement in WI-NRS scores, 6 patients experienced a ≥4-point decrease in the itch score. One patient reported no improvement, and 2 patients were lost to follow-up, with no known outcome. The mean pruritus WI-NRS score for 8 patients at their most recent visit had significantly improved to 5.38 ± 0.75 ($P < .001$). Three patients reported adverse effects from butorphanol, including insomnia, lightheadedness, and lethargy. Most patients reported no adverse events (Table II).

In addition to WI-NRS scores, the mean Dermatology Life Quality Index (DLQI) score improved from 20.22 ± 1.69 to 10.78 ± 2.99 ($n = 9$, $P = .004$). Similarly, the mean Beck's Depression Inventory (BDI) score improved from 22.11 ± 5.51 to 14.22 ± 3.80 ($n = 9$, $P = .005$), and the mean total Skindex survey scores improved from 116.44 ± 6.95 to 93.11 ± 11.76 ($n = 9$, $P = .020$).

Our study suggests that treatment with intranasal butorphanol off-label may be a therapeutic option for intractable itch that is refractory to conventional therapies. These findings corroborate previous

studies demonstrating the success of increased κ-opioid receptor expression and butorphanol use for intractable pruritus associated with inflammatory skin conditions and systemic diseases.[1,4] The most common adverse effects associated with butorphanol use include sedation, psychomotor impairment, and nausea and vomiting (Supplemental Table I, available via Mendeley at https://data.mendeley.com/datasets/pgt6tcyjp6/1). Butorphanol is a controlled substance with the potential for dependency and is thus not recommended in patients with substance use disorders.[5]

Limitations of this study include the small sample size, inconsistency in patient compliance, and the open label study design. Future large-scale trials are needed to assess the safety and efficacy of intranasal butorphanol and to determine which types of chronic pruritus benefit most from treatment.

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The role of dupilumab in the management of idiopathic chronic eczematous eruption of aging

To the Editor: Idiopathic chronic eczematous eruption of aging (CEEA) is a poorly studied subtype of eczema that affects individuals aged older than 50 years.[1,2] Although histopathology displays spongiotic dermatitis, these individuals lack a history of atopic dermatitis at any point in their past and present with a highly pruritic, subacute/chronic eczematous eruption affecting the extremities and trunk, with characteristic sparing of the face.[1,2] CEEA can be particularly disabling for older patients given its persistence, associated significant pruritus, and refractory nature to topical and systemic immunosuppressive medications.[2] Historically, patients are worked-up for other causes of an eczematous eruption, and CEEA is considered a diagnosis of exclusion.[3]

To date, we are aware of 1 case report demonstrating successful treatment of this condition with dupilumab.[1] To further explore this relationship, we evaluated 15 consecutive patients (exclusion <65 years old) with CEEA treated with dupilumab at the atopic dermatitis dose. Exclusion criteria were based on previous guidelines,[1] including history of atopic dermatitis earlier in life or other atopic disorders, pruritus without visible inflammatory skin disease, and other causes of aging-related eczematous eruptions (eg, cutaneous T-cell lymphoma, bullous pemphigoid, allergic contact dermatitis, drug eruption, and infection/infestation).

Table I summarizes demographic data of this cohort. The patients in our cohort were a mean