(OR, 1.70; 95% CI, 1.50-1.92; $P < .05$). In addition, children exposed to acetaminophen in early life seemed to have increased risk of eczema (OR, 1.21; 95% CI, 1.04-1.40; $P < .05$). We conducted separate stratified analyses based on study location (single country or multiple countries), study design (cohort study or cross-sectional study), sample size (<10,000 or ≥10,000), acetaminophen exposure at different doses and frequencies (once per year, at least once per month, or other), eczema diagnosed at different patient ages (age, <3 years, 3-7 years, or >7 to 18 years), and whether the study controlled for potential confounders (unadjusted estimates or adjusted estimates) (Table I). Factors explaining differences in the study included sample size, different dosages and durations of acetaminophen use, different patient ages at the diagnosis of eczema, and whether the studies adjusted for potential confounders (Table I).

Our meta-analysis has some limitations, such as publication bias and incomplete ascertainment of the relevant published studies. There are also some potential confounding factors, such as viral infections (which themselves could be a trigger for eczema), recall bias, and diagnosis of eczema based on parental reporting. Therefore, further investigation, including via randomized controlled studies, is needed to establish the exact association and mechanisms.

There are also some merits of our meta-analysis. First, the study featured a large sample that originated from multiple countries, which enhanced its statistical power. Second, we used a stratified analysis in the present study, which helped us to reveal the sources of the heterogeneity.

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Low-dose naltrexone therapy in benign chronic pemphigus (Hailey-Hailey disease): A case series

To the Editor: Familial benign chronic pemphigus, or Hailey-Hailey disease (HHD), is an autosomal-dominant genodermatosis. Treatment of HHD is challenging. Small case series have described the effectiveness of low-dose naltrexone (LDN).[1-3] We assessed the use of LDN in a larger series of patients with HHD.

Patients with biopsy-proven, refractory HHD controlled at the Dermatology Department of Hospital Clínic de Barcelona from November 2017 to November 2018 were proposed to receive LDN. The Institutional Review Board approved the study and written informed consent was obtained from all patients. Starting doses varied from 1.5 to 6 mg/d. Incremental doses were indicated depending on the clinical response (Table I). In some patients who were

Table I. Patient baseline characteristics and response to treatment

Patient	Sex	Age, y	Previous treatments	BSA, %	DLQI before LDN*	Disease severity†	Duration treatment, wks	Starting dose,‡ mg/d	Last/current dose,‡ mg/d	Patient response	CGIC§	PGIC§	Discontinued treatment	Reason for discontinuation	AEs
1	F	69	SC, TC, MTX, A	4	11	Moderate	3	1.5	1.5	No improvement	4	4	Yes	AE	N&D
2	F	69	TC, A, Dox	5	4	Severe	65	1.5	9.0	Initial improvement but relapsed	3	4	No		
3	F	65	TA, Dox, Ox, PDT	5	10	Severe	65	1.5	4.5	Sustained improvement	1	1	No		N&D
4	F	55	TC, TA, TT, SC	1	6	Moderate	64	1.5	3.0	Sustained improvement	1	1	No		
5	F	37	SC, Dap, TC	1	5	Mild	63	1.5	6.0	Initial improvement but relapsed	4	4	Yes	Ineffective	
6	F	54	TC, SC, TT, Tdic, Ox, Dox, Amox	5	9	Severe	55	3.0	12.0	No improvement	4	4	Yes	Ineffective	
7	F	55	A, TC, PP, TT, Tdic, Ox, Dap, Min	9	27	Severe	57	3.0	50.0	No improvement	4	4	Yes	Ineffective and AE	N&D
8	F	51	Dap, Min, Dox, PP, Ox, SC, AZA, MTX	12	22	Severe	14	3.0	3.0	No improvement	4	4	Yes	AE	N&D
9	F	62	SC, Dap, A	4	8	Moderate	35	1.5	6.0	Initial improvement but relapsed	3	3	No		
10	F	74	A, Amox, TC, Ox	9	15	Severe	29	4.5	6.0	Initial improvement but relapsed	2	3	No		
11	M	48	Dox, CO_2 laser, SC, Ox, TC, PP, Min	4	14	Severe	32	6.0	50.0	No improvement	4	4	Yes	Ineffective	
12	M	35	TC, SC, Dox, TA	4	10	Moderate	12	6.0	12.0	No improvement	4	4	No		
13	F	58	TC, A, PDT, MTX, AZA	10	15	Severe	21	3.0	3.0	Initial improvement but relapsed	3	2	No		
14	F	77	SC, Dox, TC, TA	2	5	Mild	12	6.0	6.0	Initial improvement but relapsed	3	2	No		

A, Acitretin; *AEs*, adverse events; *Amox*, amoxicillin-clavulanic acid; *AZA*, azathioprine; *BSA*, body surface area; *CGIC*, Clinician Global Impression of Change; *CO_2 laser*, carbon dioxide laser; *Dap*, dapsone; *DLQI*, Dermatology Life Quality Index; *Dox*, doxycycline; *F*, female; *LDN*, low-dose naltrexone; *M*, male; *Min*, minocycline; *MTX*, methotrexate; *N&D*, nausea and dizziness; *Ox*, oxybutynin; *PGIC*, Patient Global Impression of Change; *PDT*, photodynamic therapy; *PP*, topical potassium permanganate; *SC*, systemic corticosteroids; *TA*, topical antibiotics; *TC*, topical corticosteroids; *Tdic*, topical diclofenac; *TT*, topical tacrolimus.

*DLQI score: DLQI 0 to 1: no effect on patient's life; DLQI 2 to 5: small effect on patient's life; DLQI 6 to 10: moderate effect on patient's; DLQI 11 to 20: very large effect on patient's life; DLQI 21 to 30: extremely large effect on patient's life.

†Disease severity: severe, BSA $\geq$5% or DLQI $\geq$11; moderate, BSA 3% to 4% or DLQI 6 to 10; mild, BSA $<$3% or DLQI $\leq$ 5.

‡Doses of naltrexone administered were: 1.5, 3.0, 4.5, 6.0, 9.0, 12, 25 or 50 mg/d, depending on the patient's response.

§1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; 7, very much worse.

unresponsive to LDN, doses of 25 or 50 mg/d were prescribed, as previously described.[4] Follow-up and laboratory monitoring were performed according to clinical response.

No standardized assessment scale has been validated to date for HHD. The disease was considered severe if the patient had a body surface area (BSA) ≥5% or a dermatology life quality index (DLQI) ≥11, moderate if BSA was 3% to 4% or DLQI was 6 to 10, and mild if BSA was <3% or DLQI was ≤5. The Clinician Global Impression of Change (CGIC) and Patient Global Impression of Change (PGIC) were performed when the patient discontinued the treatment or at the cutoff point of February 2019. Patient response was classified as having no improvement, initial improvement but with relapse during follow-up, or sustained improvement (BSA <3% or DLQI ≤5 for ≥6 months).

The study included 14 patients with a median age of 56.5 years (interquartile range, 52-68 years). Patient baseline characteristics and response to therapy are summarized in Table I. Disease was severe in 8 patients. The median follow-up time was 33.6 weeks (interquartile range, 15-54 weeks). Six patients had a follow-up of >1 year and 3 of >6 months. Six patients showed no improvement with LDN, and 6 had an initial improvement but relapsed. Two patients had a sustained response of >1 year. Six patients discontinued the treatment, 4 because of ineffectiveness and 2 because of adverse events.

Most publications of HHD treated with LDN describe a reduced number of patients with variable follow-up time. In our study, the largest series described to date, we observed a lack of response or an initial response with subsequent relapse in most patients. In patients who had a relapse, there was a mild to moderate improvement with the treatment, according to the CGIC and PGIC, probably as a result of a decrease in the intensity and duration of flares. Only 2 patients, with follow-up of >1 year, showed sustained improvement. Interestingly, these 2 patients are sisters. Further studies are required to determine whether certain mutations[5] can be associated with favorable responses to LDN. Patients showed a response to treatment mainly on doses of 3.0 and 4.5 mg/d. Increasing the dose of naltrexone to 25 or 50 mg/d, did not seem to offer better results in our patients.

LDN may be an alternative in patients with refractory HHD, although with lower response rates than those described, with frequent relapses.

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A pilot study of 2% tofacitinib cream with narrowband ultraviolet B for the treatment of facial vitiligo

To the Editor: Current treatments for vitiligo are limited in efficacy, often producing suboptimal results. Recent studies have established that $CD8^+$ T-cell and interferon γ signaling, mediated by the Janus kinase (JAK)−signal transducer and activator of transcription pathway, contribute to the pathogenesis of vitiligo.[1] JAK inhibitors block this pathway and are currently Food and Drug Administration approved for autoimmune diseases,