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Research letter

The use of hydroxychloroquine as a systemic treatment in erosive lichen planus of the vulva and vagina

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DEAR EDITOR, Erosive lichen planus affecting the vulva and vagina (ELPV) is a rare inflammatory skin disease, presenting with painful erosions and severe scarring.¹ The disease course is persistent and often refractory to treatment: up to 45% of patients do not experience remission with topical treatments, and evidence for systemic treatments remains scarce.² Hydroxychloroquine (HCQ) is frequently used in daily practice as a first choice systemic therapy.³ However, little evidence is available on use of HCQ for ELPV.² The aim of this study was to analyse the effectiveness and safety of HCQ in ELPV.

Adult patients diagnosed with ELPV and treated with HCQ between 2009 and 2020 were retrospectively analysed. Patients with insufficient clinical data, or patients who made a general objection to the use of their data in research were excluded. Informed consent was not collected, because of anonymous data processing and lack of care regimen interference. Due to this study's noninterventional character, the Medical Research Involving Human Subjects Act did not apply, and official approval by the medical ethics review committee was not required.

Clinical response was analysed using the Physician's Global Assessment score. Clinical response was defined as a decrease in physical signs for at least two consecutive hospital visits. A flare-up was defined as return to baseline disease activity or worsening of physical signs after initial response. Adverse events (AE) were graded in severity with the Common Terminology Criteria for Adverse Events (CTCAE).⁴

A total of 15 patients with ELPV treated with HCQ were analysed. Beforehand, five patients were excluded, because of insufficient clinical data ($n = 4$, all follow-up in a different hospital) and HCQ being used for another indication ($n = 1$). The median age was 55 years (range 23–82) and 67% were postmenopausal. The median diagnostic delay was 2 years (range 0–11). Overall, 87% ($n = 13$) had biopsy-proven lichen planus, nine of which were based on vulval biopsy. Other biopsy sites included the oral mucosa and skin. Oral lichen planus was present in 53% ($n = 8$).

Fourteen patients used concomitant topical treatment, mainly tacrolimus 0.01% ointment (47%), topical steroids (67%) and hydrocortisone/estriol vaginal creams (27%). HCQ was the first systemic treatment in 11 patients, whereas four

had received one or more immunosuppressive drugs before, which were HCQ ($n = 2$), prednisolone ($n = 2$), methotrexate ($n = 1$) and ciclosporin ($n = 1$).

In this study, HCQ dosage, dependent on disease activity and tolerance, ranged between 200 and 600 mg, with one outlier of 800 mg in a patient who was a 'nonresponder'. In total, 60% ($n = 9$) responded to HCQ. At 3 months, all patients were still on HCQ, with three patients reporting improvement. At nine months, twelve patients were still on HCQ, with eight reporting improvement. Seven (47%) patients were still successfully on HCQ at 24 months. Reported dosages at initial response were 400 mg ($n = 7$) and 200 mg ($n = 2$). Further dose–response correlations could not be evaluated because of individual dosage fluctuations. Patients visited with a median 3-month interval (range 0.6–12.6). The median time to treatment response was 5 months (range 1–18.5). Median treatment duration was 23.8 months (range 4.1–81). Reasons for cessation included ineffectiveness ($n = 6$), AE ($n = 1$), development of malignancy ($n = 1$) and loss to follow-up ($n = 2$).

Three patients (20%) experienced disease flare-ups during treatment. Flare-ups resolved spontaneously or after dosage increase after a median of 11 weeks (range 2.8–31.3). Eight patients (53%) experienced AEs during treatment, most commonly infections and gastrointestinal complaints. AEs resolved after dosage lowering or additional treatment (Table 1).

Previous research has shown that ELPV is a difficult to treat condition.^{2,3} This study suggests that HCQ can be an effective treatment in ELPV. Overall, 60% of the patients responded to HCQ, with almost half experiencing a long-term effect. AEs (53%) were mostly mild or moderate. Flare-ups (20%) resolved either after dosage increase or spontaneously.

Our response rate to HCQ was higher compared with the 36% success rate of a case audit review in ELPV.³ Unfortunately, no dosages were described, making comparison difficult. Recently, Cline *et al.* reported a clinical improvement of 70% with methotrexate in ELPV,⁵ exceeding our response rate. However, HCQ was better tolerated: only one patient stopped because of an AE, compared with 30% from methotrexate use.

Our results suggest that HCQ has a slow onset of action, as only 20% reported improvement at 3 months, but 53% had responded at 9 months. The time taken to respond may be overestimated, as data were collected retrospectively during hospital visits.

Limitations include the retrospective nature, the limited heterogeneous sample size and use of concomitant topical medication.

Table 1 Treatment characteristics of 15 patients with erosive lichen planus affecting the vulva and vagina

Treatment characteristics (n = 15)	Values
Dosage in mg/day, range	200–800
HCQ duration in months, median (range)	23.8 (4.1–81)
Total follow-up duration in months, median (range)	38 (4–123)
Time until response in months, median (range)	5 (1–18.5)
Responders	9 (60)
3 months	3 (20)
9 months	8 (53)
12 months	7 (47)
24 months	7 (47)
Patients with flare-ups	3 (20)
Flare-up duration in weeks, median (range)	11 (2.8–31.3)
Concomitant topical anti-inflammatory treatment	14 (93)
Topical corticosteroids	10 (67)
HCA 2.5%/estriol vaginal cream	4 (27)
Topical tacrolimus 0.1% ointment	7 (47)
Intralesional steroid injections	1 (7)
Experienced AE	8 (53)
Hearing loss (CTCAE 3)	1 (7)
Nausea (with weight loss) (CTCAE 2)	1 (7)
Infection (CTCAE 2)	3 (20)
Blurry vision (CTCAE 2)	1 (7)
Gastrointestinal disturbances (CTCAE 1)	3 (20)
Dizziness (CTCAE 1)	3 (20)
Infections (CTCAE 1)	2 (13)
Headache (CTCAE 1)	2 (13)
Fatigue (CTCAE 1)	1 (7)
Heart palpitations (CTCAE 1)	1 (7)
Hair loss (CTCAE 1)	1 (7)
Tinnitus (CTCAE 1)	1 (7)
General malaise (CTCAE 1)	1 (7)

Data are n (%) unless otherwise specified. AE adverse event; CTCAE, Common Terminology Criteria for Adverse Events (CTCAE grade 1–5: mild, moderate, severe, life-threatening, death); HCA, hydrocortisone; HCQ hydroxychloroquine.

Although evidence about systemic treatment in ELPV is scarce, this study provides a broad view on treatment characteristics and safety of HCQ in ELPV in a daily care setting.²

We conclude that HCQ can be an effective and safe treatment in ELPV. Future studies are needed to further assess effective systemic treatments for ELPV.

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