Hydroxychloroquine Reduces Proteinuria in Indian Patients With IgA Nephropathy

To the Editor: Initial supportive treatment of IgA nephropathy (IgAN) consists of salt restriction, renin-angiotensin system (RAS) blockade, and blood pressure control. The Kidney Disease: Improving Global Outcomes guidelines[1] suggest that hydroxychloroquine (HCQ), an antimalarial agent with immunomodulatory effects, may be used in Chinese patients,[2–4] but there is paucity of data in other ethnicities. HCQ is widely used in the treatment of autoimmune diseases. Its inhibitory effect on Toll-like receptors has generated interest as Toll-like receptor 9 has been implicated in the pathogenesis of IgAN.[5]

We describe our experience with HCQ in Indian patients with IgAN (Supplementary Methods). A total of 38 patients with primary IgAN having persistent proteinuria >1 g/d despite supportive treatment had received HCQ for 6 months (details in Supplementary Methods section). One patient had discontinued treatment immediately because of persistent gastritis, and 37 cases were analyzed (Table 1). Mean estimated glomerular filtration rate (eGFR) was 74.7 ± 27.4 ml/min per 1.73 m^2, and proteinuria was 2.1 ± 0.8 g/d. Of 37 patients, 21 (56.8%) achieved remission of proteinuria (complete remission: 10, partial remission: 11) after 6 months of HCQ treatment. None had >40% decline in estimated glomerular filtration rate or progression to end-stage renal failure. Those who achieved remission had higher proteinuria than nonresponders though not statistically significant (2.5 ± 0.9 g/d vs. 1.8 ± 0.4 g/d, respectively). In a randomized controlled trial[2] in Chinese patients, HCQ was significantly superior to placebo in reducing proteinuria ($P < 0.001$). In a systematic review, HCQ was more effective in reducing proteinuria compared with supportive treatment but not compared with immunosuppression.[5] Furthermore, 8 patients (21.6%) in our cohort relapsed after discontinuation of HCQ during a median follow-up of 22.0 (7.4–27.6) months; 4 achieved remission after restarting HCQ whereas 3 had persistent proteinuria. There is no information about relapse in previous studies.[2,3] Apart from 1 patient who discontinued treatment initially, no other adverse effects were reported.

Thus, HCQ can be considered for supportive management of IgAN in those who do not respond to renin-angiotensin system blockade before prescribing immunosuppression. It is inexpensive, well tolerated, and not associated with increased incidence of infections. The risk of relapse suggests that longer duration of treatment may be warranted as is done in lupus nephritis. Further prospective studies are needed in different ethnicities to determine the category of patients who are most likely to benefit with this drug and the long-term effects on renal survival.

Table 1. Baseline characteristics of patients at the time of initiation of hydroxychloroquine

Baseline characteristics	Total patients ($N = 37$)
Age (yr) (mean ± SD)	35.1 ± 9.1
Males (%)	23 (62.2)
Hypertension (%)	27 (73)
Urinary protein (gg/d) (mean ± SD)	2.1 ± 0.8
Hematuria (%)	19 (51.4)
Serum creatinine (mg/dl) (mean ± SD)	1.4 ± 0.4
eGFR (ml/min per 1.73 m^2) (mean ± SD)	74.7 ± 27.4
Serum albumin (mg/dl) (mean ± SD)	3.9 ± 0.3
MEST-C lesions (%)	
M1	30 (81.1)
E1	1 (0.03)
S1	29 (78.4)
T1/T2	15 (40.5)
C1	6 (16.2)

eGFR, estimated glomerular filtration rate.

ACKNOWLEDGMENTS

The authors thank Mr. Dinesh Jain (SRF) for his assistance in the follow-up of the patients.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

1. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. *Kidney Int*. 2021;100:S1–S276.
2. Liu LJ, Yang YZ, Shi SF, et al. Effects of hydroxychloroquine on proteinuria in IgA nephropathy: a randomized controlled trial. *Am J Kidney Dis*. 2019;74:15–22. https://doi.org/10.1053/j.ajkd.2019.01.026
3. Yang YZ, Chen P, Liu LJ, et al. Comparison of the effects of hydroxychloroquine and corticosteroid treatment on proteinuria in IgA nephropathy: a case-control study. *BMC Nephrol*. 2019;20:297. https://doi.org/10.1186/s12882-019-1488-6
4. Stefan G, Mircescu G. Hydroxychloroquine in IgA nephropathy: a systematic review. *Ren Fail*. 2021;43:1520–1527. https://doi.org/10.1080/0886022X.2021.2000875
5. Suzuki H, Suzuki Y, Narita I, et al. Toll-like receptor 9 affects severity of IgA nephropathy. *J Am Soc Nephrol*. 2008;19:2384–2395. https://doi.org/10.1681/ASN.2007121311

Soumita Bagchi[1], Dipankar Bhowmik[1], Geetika Singh[1] and Sanjay Kumar Agarwal[1]

[1]Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India

Correspondence: Soumita Bagchi, Department of Nephrology, All India Institute of Medical Sciences, New Delhi, India. E-mail: soumita_bagchi@yahoo.co.in

Received 1 April 2022; revised 12 April 2022; accepted 18 April 2022; published online 26 April 2022

Kidney Int Rep (2022) **7,** 1443–1444; https://doi.org/10.1016/j.ekir.2022.04.086