Hydroxychloroquine Efficacy and Safety in Patients With Systemic Lupus Erythematosus: A Retrospective Cohort Comparing 200 mg Versus 400 mg

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Outline

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- Literature Review
- Objectives
- Methodology
- Results
- Conclusion

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease in which the immune system attacks its own tissues, causing inflammation and tissue damage in the affected organs.

SLE is Caused by: environmental, genetic, and hormonal factors.

Hydroxychloroquine (HCQ) is the mainstay in the treatment of SLE.

Side effects include: retinal, neuromuscular and cardiac manifestations with **retinopathy** being the most concerning.

SLE: Systemic Lupus Erythematosus, HCQ: Hydroxychloroquine

Literature Review

(Petri et al., 2020)

Meta Analysis

- HCQ associated retinopathy was rare; only 12 patients out of 4,415 patients developed retinopathy.

(Ruiz-Irastorza et al., 2010)

Systematic Review

- HCQ can prevent lupus flares and increase long-term survival. Toxicity of was infrequent, mild and often reversible.

(Costedoat-Chalumeau et al., 2013)

RCT

- No differences were seen between groups in terms of nausea, vomiting, diarrhea or blurred vision. No severe side effects were detected.

HCQ: Hydroxychloroquine, RCT: Randomized controlled trial

Significance and Aim

Safety and Efficacy	Importance of Optimal Control
Inconsistent Evidence	Reduced morbidity
200 mg and 400 mg	Reduced mortality

Aim

To investigate the efficacy and safety of these two different regimens in SLE patients.

Objectives

Primary Objective

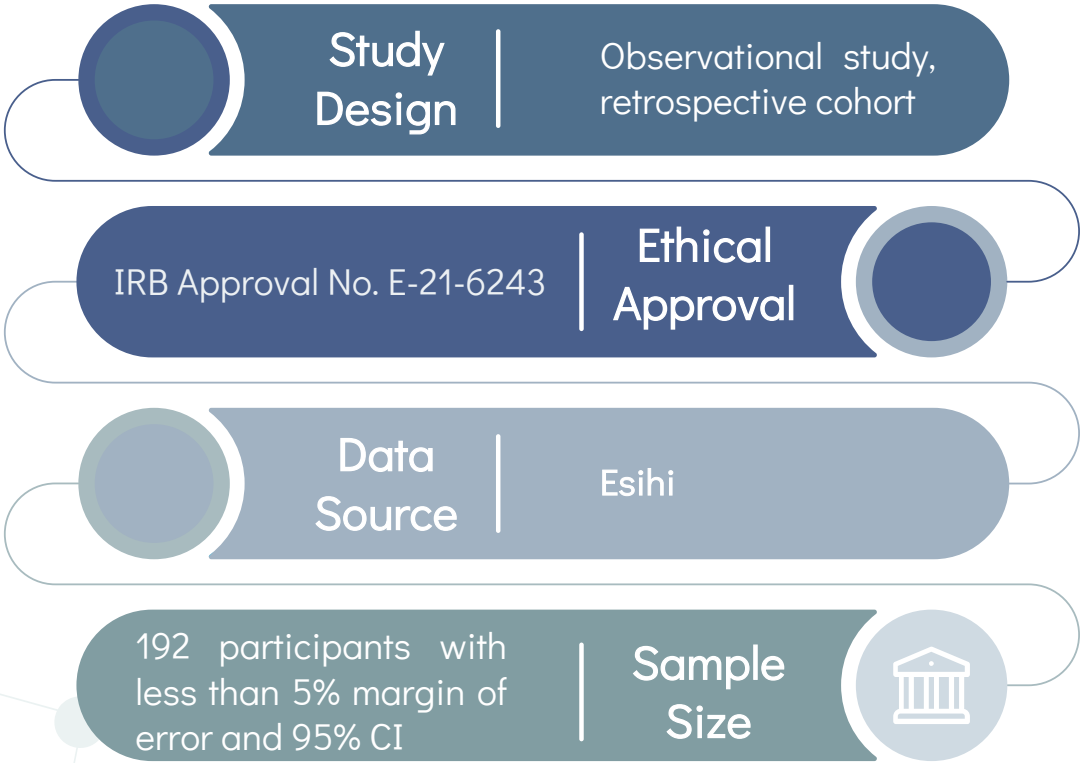
- To investigate the different dosing regimens (200 mg and 400 mg) of HCQ in SLE patients in terms of efficacy and safety.

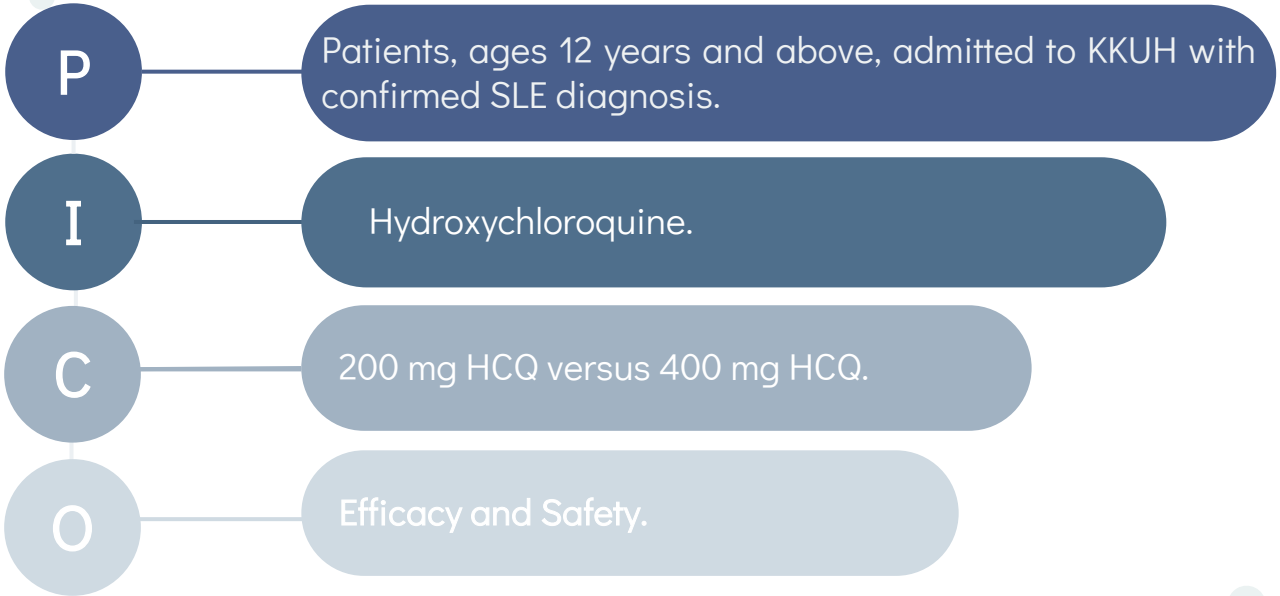
Secondary Objective

- To determine number of patients who experienced flares and corresponding doses.
- To determine number of admissions related to SLE.

SLE: Systemic Lupus Erythematosus, HCQ: Hydroxychloroquine

Methodology


Study Design
Observational study, retrospective cohort
IRB Approval No. E-21-6243
Ethical Approval
Data Source
Esihi
192 participants with less than 5% margin of error and 95% CI
Sample Size



SLE: Systemic Lupus Erythematosus, HCQ: Hydroxychloroquine

Outcome Measures

Primary Outcome

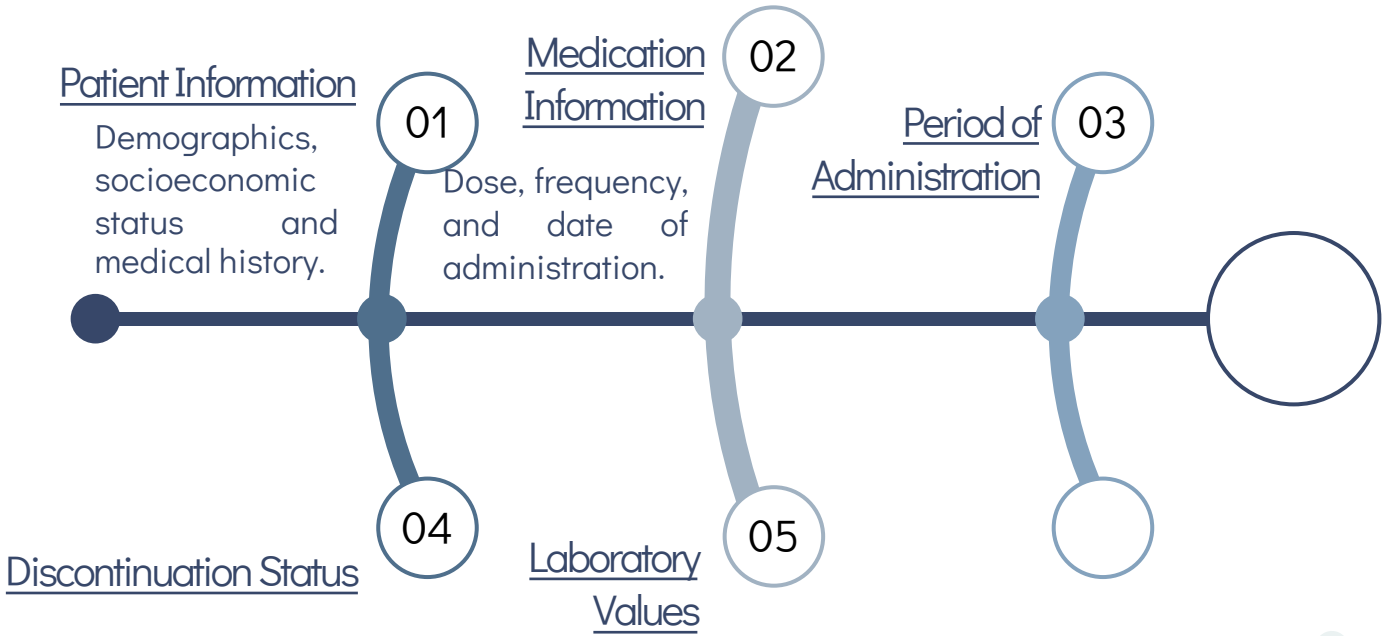
Assess efficacy by hospital admissions and labs (Hematuria & proteinuria).

Secondary Outcome

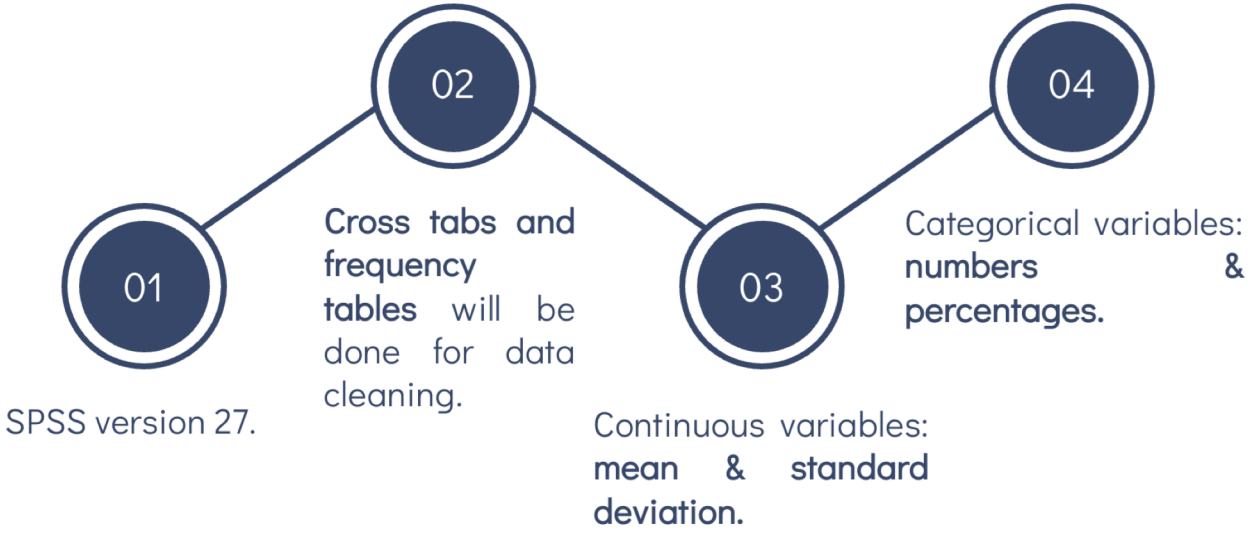
Assess safety by measuring labs (ALT, AST, WBC & Scr).

ALT: Alanine transaminase, AST: Aspartate transaminase, WBC: White blood cells, SCR: Serum creatinine

Variables


Patient Information
01
Demographics, socioeconomic status and medical history.
Medication Information
02
Dose, frequency, and date of administration.
Period of Administration
03
Discontinuation Status
04
Laboratory Values
05

Statistical Methods



Results

Table 1 baseline demographics and univariate analysis

		200 mg N, (%)	400 mg N, (%)	Alternate dosing N, (%)	Total N, (%)	P value
Gender	Male	10, (90.0%)	1, (9.1%)	0, (0.0%)	11, (10.2%)	0.698
	Female	79, (81.4%)	15, (15.5%)	3, (3.1%)	97, (89.8%)	
Age (years)	Mean, (SD)	47, (12)	49, (11)	49, (11)	48, (12)	0.915
Body mass index (Kg/m2)	Mean, (SD)	32.88, (35.75)	32.26, (6.78)	25.80, (0.22)	32.59, (32.65)	0.935
Nationality	Saudi	84, (82.4%)	15, (14.7%)	3, (2.9%)	102, (94.4%)	0.909
	Non Saudi	5, (83.3%)	1, (16.7%)	0, (0.0%)	6, (5.6%)	
Education	Not documented	89, (83.2%)	15, (14.0%)	3, (2.8%)	107, (99.1%)	0.055
	High	0, (0.0%)	1, (100.0%)	0, (0.0%)	1, (0.9%)	
Marital status	No	31, (81.6%)	5, (13.2%)	2, (5.3%)	38, (35.2%)	0.492
	Yes	58, (82.9%)	11, (15.7%)	1, (1.4%)	70, (64.8%)	
	Unknown	0, (0.0%)	0, (0.0%)	0, (0.0%)	0, (0.0%)	
Employment	No	0, (0.0%)	0, (0.0%)	0, (0.0%)	0, (0.0%)	0.642
	Yes	4, (100.0%)	0, (0.0%)	0, (0.0%)	4, (3.7%)	
	Not documented	85, (81.7%)	16, (15.4%)	3, (2.9%)	104, (96.3%)	

Table 2 comorbidities and univariate analysis

		200 mg N, (%)	400 mg N, (%)	Alternate dosing N, (%)	Total N, (%)	P value
Hypertension	No	58, (82.9%)	10, (14.3%)	2, (2.9%)	70, (64.8%)	0.977
	Yes	31, (81.6%)	6, (15.8%)	1, (2.6%)	38, (35.2%)	
Diabetes mellitus	No	78, (83.0%)	13, (13.8%)	3, (3.2%)	94, (87.0%)	0.622
	Yes	11, (78.6%)	3, (21.4%)	0, (0.0%)	14, (13.0%)	
Dyslipidemia	No	83, (83.8%)	14, (14.1%)	2, (2.0%)	99, (91.7%)	0.211
	Yes	6, (66.7%)	2, (22.2%)	1, (11.1%)	9, (8.3%)	
Type of organ affected	No major organ involvement / NA	39, (83.0%)	7, (14.9%)	1, (2.1%)	47, (43.5%)	0.949
	Nephritis	35, (83.3%)	6, (14.3%)	1, (2.4%)	42, (38.9%)	
	Cutaneous	10, (71.4%)	3, (21.4%)	1, (7.1%)	14, (13.0%)	
	Cerebritis	3, (100%)	0, (0.0%)	0, (0.0%)	3, (2.8%)	
	Nephritis and cerebritis	2, (100%)	0, (0.0%)	0, (0.0%)	2, (1.9%)	
Class of organ involvement	Not mentioned	53, (81.5%)	10, (15.4%)	2, (3.1%)	65, (60.2%)	0.94
	Mild I-II	7, (87.5%)	1, (12.5%)	0, (0.0%)	8, (7.4%)	
	Moderate III-IV	17, (77.3%)	4, (18.2%)	1, (4.5%)	22, (20.4%)	
	Severe V	12, (92.3%)	1, (7.7%)	0, (0.0%)	13, (12.0%)	

Table 3 primary outcome variables for safety and efficacy

	200 mg		400 mg		Alternate dosing		Total		
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	P value
Safety									
Number of hospitalizations (total)	2	3	2	3	2	3	2	3	0.627
ALT1 (unit/L)	23.54	9.28	31.27	30.52	19	8.54	24.6	14.7	0.14
AST1 (unit/L)	19.17	7.04	18.29	9.9	15.33	3.21	18.92	7.4	0.643
WBC1 $x10^9$	43.28	332.64	6.86	3.57	4.9	1.82	36.3	299.38	0.893
SCR1 (mcmol/L)	66.42	42.55	66.73	13.87	73.67	50.86	66.7	39.39	0.953
ALT2 (unit/L)	23.88	10.21	25.38	8.92	26.67	15.31	24.22	10.07	0.792
AST2 (unit/L)	19.05	6.65	18.5	3.95	19	11.53	18.96	6.37	0.952
WBC2 $x10^9$	41.62	326.68	338.29	1289.63	4.73	1.07	84.16	574.04	0.179
SCR2 (mcmol/L)	66.93	57.59	59.85	9.48	69	41.87	66.04	53.08	0.903
ALT3 (unit/L)	25.77	17.16	24.47	7.74	21.5	10.61	25.48	15.92	0.901
AST3 (unit/L)	19.33	9.68	17.79	11.36	18.33	7.77	19.08	9.8	0.857
WBC3 $x10^9$	5.89	2.5	6.32	3.24	3.75	0.49	5.91	2.59	0.421
SCR3 (mcmol/L)	67.76	49.09	57.2	16.26	62.67	39.43	66.04	45.38	0.707
Efficacy									
Number of hospitalization related to SLE	1	2	2	2	0	0	1	2	0.353
Total number of days hospitalized for SLE	5	12	4	4	0	0	5	10	0.736

ALT: Alanine transaminase, AST: Aspartate transaminase, WBC: White blood cells, SCR: Serum creatinine, SLE: Systemic lupus erythematosus

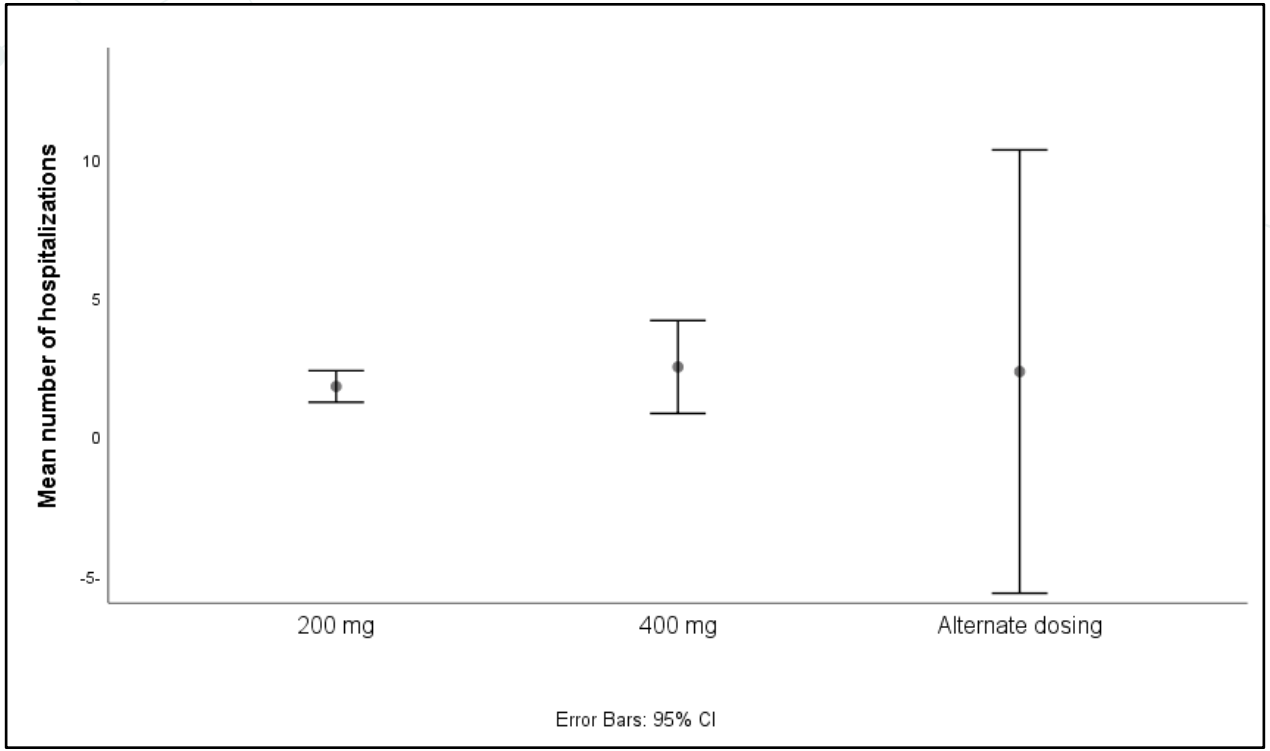


Figure 1 number of total hospitalizations by HCQ dose

HCQ: Hydroxychloroquine

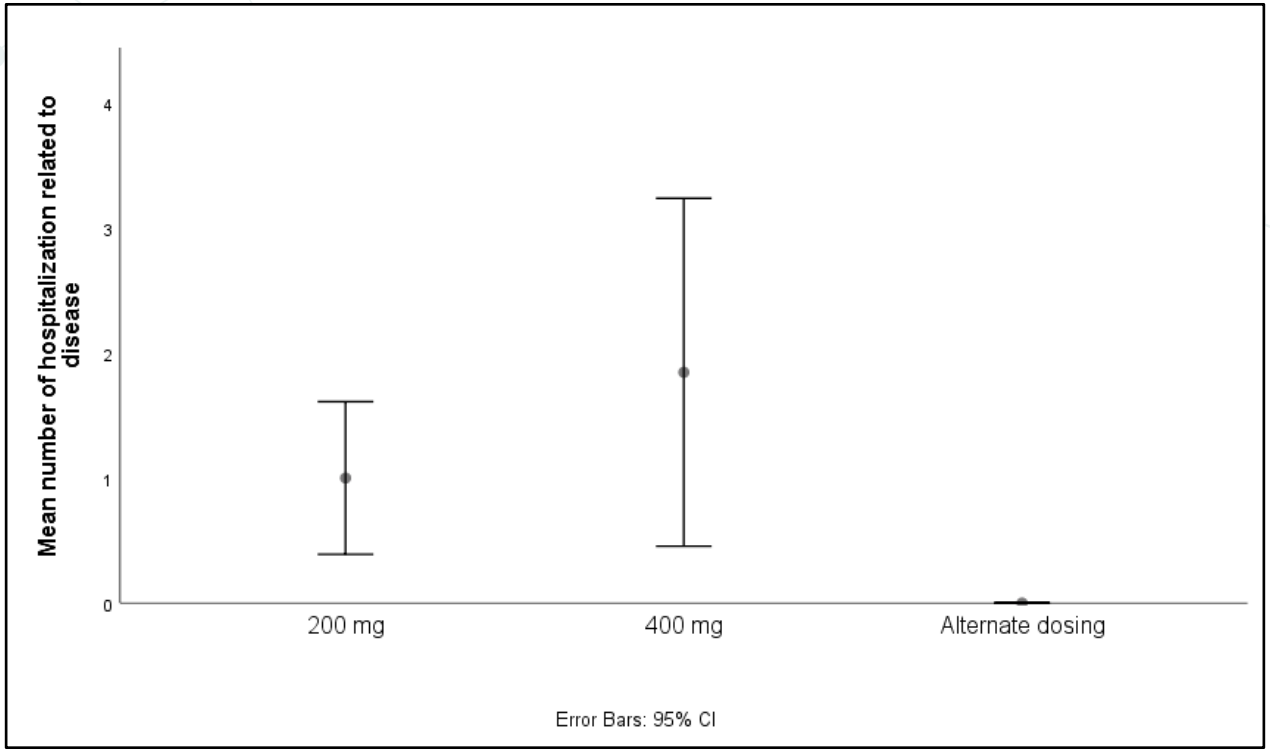


Figure 2 number of hospitalizations related to SLE indicating efficacy by HCQ

SLE: Systemic Lupus Erythematosus, HCQ: Hydroxychloroquine

Table 4 efficacy demonstrated by labs

		200 mg N, (%)	400 mg N, (%)	Alternate dosing N, (%)	Total N, (%)	P value
Hematuria at first dose	Negative	46, (83.6%)	8, (14.5%)	1, (1.8%)	55, (80.9%)	
	Trace (10-20)(0-0.3)	5, (83.3%)	1, (16.7%)	0, (0.0%)	6, (8.8%)	
	1+(30-70)(0.06-0.1)	5, (100.0%)	0, (0.0%)	0, (0.0%)	5, (7.4%)	0.795
	2+(100-200)	1, (50.0%)	1, (50.0%)	0, (0.0%)	2, (2.9%)	
	3+(300-600)(>=1)	0, (0.0%)	0, (0.0%)	0, (0.0%)	0, (0.0%)	
Proteinuria at first dose	Negative	39, (83.0%)	7, (14.9%)	1, (2.1%)	47, (67.1%)	
	Trace (10-20)(0-0.3)	13, (86.7%)	2, (13.3%)	0, (0.0%)	15, (21.4%)	
	1+(30-70)(0.06-0.1)	2, (66.7%)	1, (33.3%)	0, (0.0%)	3, (4.3%)	0.972
	2+(100-200)	3, (100.0%)	0, (0.0%)	0, (0.0%)	3, (4.3%)	
	3+(300-600)(>=1)	2, (100.0%)	0, (0.0%)	0, (0.0%)	2, (2.9%)	
Hematuria at mid duration	Negative	48, (80.0%)	11, (18.3%)	1, (1.7%)	60, (72.3%)	
	Trace (10-20)(0-0.3)	15, (88.2%)	1, (5.9%)	1, (5.9%)	17, (20.5%)	
	1+(30-70)(0.06-0.1)	2, (100.0%’	0, (0.0%)	0. (0.0%)	2, (2.4%)	0.872
	2+(100-200)	2, (66.7%)	1, (33.3%)	0, (0.0%)	3, (3.6%)	
	3+(300-600)(>=1)	1, (100.0%)	0, (0.0%)	0, (0.0%)	1, (1.2%)	
Proteinuria at mid duration	Negative	42, (91.3%)	4, (8.7%)	0, (0.0%)	46, (55.4%)	
	Trace (10-20)(0-0.3)	12, (66.7%)	5, (27.8%)	1, (5.6%)	18, (21.7%)	
	1+(30-70)(0.06-0.1)	11, (73.3%)	3, (20.0%)	1, (6.7%)	15, (18.1%)	0.097
	2+(100-200)	3, (100.0%)	0, (0.0%)	0, (0.0%)	3, (3.6%)	
	3+(300-600)(>=1)	0, (0.0%)	1, (100.0%)	0, (0.0%)	1, (1.2%)	
Hematuria at last recorded lab	Negative	27, (77.1%)	7, (20.0%)	1, (2.9%)	35, (64.8%)	
	Trace (10-20)(0-0.3)	13, (86.7%)	2, (13.3%)	0, (0.0%)	15, (27.8%)	
	1+(30-70)(0.06-0.1)	2, (100.0%)	0, (0.0%)	0, (0.0%)	2, (3.7%)	0.847
	2+(100-200)	0, (0.0%)	0, (0.0%)	0, (0.0%)	0, (0.0%)	
	3+(300-600)(>=1)	1, (50.0%)	1, (50.0%)	0, (0.0%)	2, (3.7%)	
Proteinuria at last recorded lab	Negative	22, (88.0%)	3, (12.0%)	0, (0.0%)	25, (49.0%)	
	Trace (10-20)(0-0.3)	12, (80.0%)	3, (20.0%)	0, (0.0%)	15, (29.4%)	
	1+(30-70)(0.06-0.1)	3, (50.0%)	2, (33.3%)	1, (16.7%)	6, (11.8%)	0.137
	2+(100-200)	4, (80.0%)	1, (20.0%)	0, (0.0%)	5, (9.8%)	
	3+(300-600)(>=1)	0, (0.0%)	0, (0.0%)	0, (0.0%)	0, (0.0%)	

Strengths and Limitations

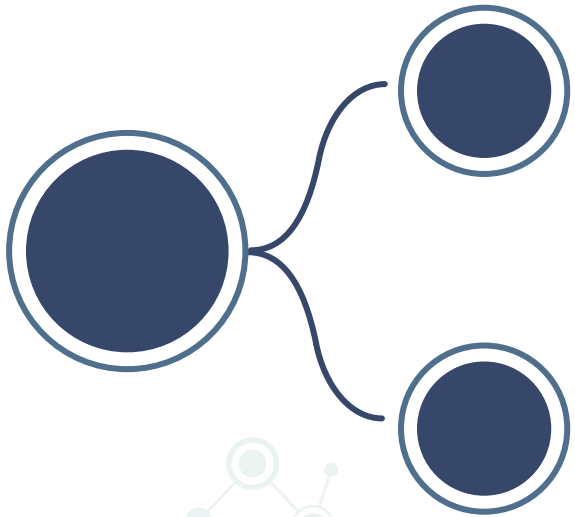
- First study of it's kind in **Saudi Arabia** to compare the efficacy and safety of an important medication in the management of SLE.
- Longitudinal study design.

- Retrospective observational nature of the study.
- Single centered study.

SLE: Systemic Lupus Erythematosus

Conclusion

Conclusion



Despite the slight differences between the two regimens, our study shows no significance.

More studies with larger sample size are needed to compare the different dosing regimens of HCQ in the future.

HCQ: Hydroxychloroquine

Thank You For Listening!

Any Questions?

References