

## A PROSPECTIVE OBSERVATIONAL STUDY ON SAFETY AND EFFICACY OF HYDROXYCHLOROQUINE AGAINST DICLOFENAC IN OSTEOARTHRITIS

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### ABSTRACT

**Objective:** The main aim of this study is to compare the effectiveness of treatment of osteoarthritis (OA) with hydroxychloroquine against diclofenac and to compare the safety of the treatment of OA with hydroxychloroquine against diclofenac. The secondary objectives are the comparison of onset and duration of action of both the treatments.

**Methods:** A prospective interventional study has been done in a tertiary care teaching hospital for 1 year from January 2016 to December 2016. The interventional model included an active control (diclofenac - nonsteroidal anti-inflammatory drugs). The control group received diclofenac 75 mg for 12 weeks, whereas the test group received hydroxychloroquine 200 mg for 3 months.

**Results:** Pain control is significantly rapid in diclofenac group, whereas the duration of action is significantly increased in hydroxychloroquine. It can be clearly seen that the hydroxychloroquine group significantly increases the quality of life when compared to diclofenac group. It is clearly seen that the incidence of gastric ulcers is more common in diclofenac group when compared to hydroxychloroquine group.

**Conclusion:** Hydroxychloroquine offers a newer spectrum in the management of OA. Although it is slow acting, it has significantly increased the quality of patient as it can have a prolonged action. Hence, hydroxychloroquine can be used as a newer entity in the management of OA.

**Keywords:** Osteoarthritis, Hydroxychloroquine, Diclofenac.

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### INTRODUCTION

Osteoarthritis (OA) is the most widespread type among arthritis, triggering a considerable joint aches and fragility. OA is one of the chief reasons of health-care outflow, and its occurrence will further upsurge with the old-age people. Existing treatments for OA have significant restrictions and novel analgesic therapies are required. Synovitis is predominant in OA and is usually accompanied with pain. For treating synovitis in inflammatory arthritis, the hydroxychloroquines are used [1].

Hydroxychloroquine is an aminoquinolone primarily an antimalarial drug. It inhibits movement of neutrophils and chemotaxis of eosinophils and damages complement-associated antigen-antibody reactions [2,3].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are enzyme inhibitors. They block cyclooxygenase (COX-1 and COX-2 enzymes), which is liable for the production of prostaglandins and thromboxane [4,5].

#### Aim

The main aim is to compare the effectiveness of treatment of OA with hydroxychloroquine against diclofenac and to compare the safety of treatment of OA with hydroxychloroquine against diclofenac. The secondary objectives are the comparison of onset and duration of action of both the treatments.

### METHODS

#### Sample size

Sample size was estimated with a prevalence of 100 patients. The estimated sample size with a confidence interval of 95% was found to be 80 with a 2.75% margin of error.

#### Study design

A prospective interventional study has been carried out in a tertiary care hospital for 1 year from January 2017 to December 2017. The interventional model included an active control (diclofenac - NSAIDs).

#### Patient selection

##### Inclusion criteria

The following criteria were included in the study:

- Patients of both sexes above the age of 18 years.
- Patients diagnosed with OA.
- Patients who fulfill the criteria for OA as per the American College of Rheumatology.

##### Exclusion criteria

The following criteria were excluded from the study:

- Pregnant and nursing women.
- People diagnosed with multiple inflammation.
- People diagnosed with rheumatoid arthritis or have positive rheumatoid antigen.
- Patients who are known case of malaria at the time of inclusion.
- Patients with serum uric acid levels above 6.8 mg/day.

An informed consent has been obtained from all the included patients. Patients' confidentiality has been maintained throughout this study. The work has been approved by the Institutional Ethics Committee IEC/VELS/DOPV/2016/33.

A specially designed pro forma has been utilized to carry out this study. Patients demographics such as age, sex, laboratory values, patient medical history etc were collected. The patient was followed up for every month.

The control group received diclofenac 75 mg for 12 weeks, whereas the test group received hydroxychloroquine 200 mg BD for 3 months. Patients' quality of life is measured before the initiation of the study as well as the conclusion of 3 months. Standard validated SF-12 questionnaire is administered before and after the end of intervention. Physical and mental component scoring was assessed. Laboratory data such as erythrocyte sedimentation rate were estimated to compare the efficacy.

### Statistical analysis

One sample student *t*-test was used to compare the quality of life among the patients. Chi-squared test was used to compare the control of 95% and a *p*<0.05 is considered to be statistically significant.

## RESULTS

The following results were obtained in the study.

Table 1 shows that female are more prone to OA when compared to male distribution.

Table 2 shows that patients between 50 and 65 years of age are more prone to OA when compared to other age distribution.

**Table 1: Gender distribution**

Gender	Number of patients (%)
Male	16 (25)
Female	64 (75)

**Table 2: Age distribution**

Age group (n=80)	Number of patients (%)
18-35 years	8 (10)
35-50 years	20 (25)
50-65 years	36 (45)
>65 years	16 (20)

**Table 3: OA type**

OA type	Number of patients (%)
Knee	72 (90.00)
Hip	6 (7.50)
Hand	2 (2.50)

OA: Osteoarthritis

**Table 4: Comorbidities**

Comorbidity	Number of patients (%)
DM	24 (30.00)
HTN	20 (25.00)
BA	7 (8.75)
Dyslipidemia	3 (3.75)
No comorbidities	12 (15.00)

DM: Diabetes mellitus

Table 3 shows that knee OA patients are more prone when compared to other types.

Table 4 shows that diabetes mellitus (DM) patients are more prone to OA when compared to other comorbidities (Tables 5-8).

Pain control is significantly rapid in diclofenac group, whereas the duration of action is significantly increased in hydroxychloroquine.

It can be clearly seen that the hydroxychloroquine group significantly increases the quality of life when compared to diclofenac group.

It is clearly seen that the incidence of gastric ulcers is more common in diclofenac group when compared to hydroxychloroquine group.

## DISCUSSION

In general, women are more prone to the OA when compared to the men. Specialist's assessment is that almost 60% of the women in the US are having OA. Similar patterns were reported in our study.

The anatomy of a female's physique is organized in such a way which may show a part in her risk for OA of the knees. Specifically, woman tends to have broader hips, in which some specialists' belief affects the position of the knee and causes irregular stress on the knees, leading to OA [6].

As age increases, the highest risk factor for OA is also increases, and it is not an unavoidable magnitude of getting aged. The elderly changes in joint tissues that fund to the growth of OA include cell senescence that fallouts in the expansion of the senescent secretory phenotype and aging variations in the matrix, including the development of progressive glycation end products that affect the mechanical possessions of joint tissues [7,8].

Knee OA is of additional importance not only for its significant occurrence rate related with other forms of OA but also for its appearance at earlier age groups predominantly in younger age groups of overweight women. The incidence of knee OA increases by age and further increases with lengthier lifetime and advanced usual weight of the population [9].

DM and hyperglycemia are correlated with OA in some epidemiological studies. Moreover, the relationship within the two diseases might be supported by the lethal role of glucose spare through the buildup of advanced glycation end products, oxidative stress, and promotion of systemic inflammation [10,11].

Hydroxychloroquine blocks the action of certain chemical messengers that are responsible for inflammation, swelling, and redness associated with certain joint diseases. Although it is slow acting, duration of the action of hydroxychloroquine is more when compared to diclofenac (NSAIDs).

Diclofenac spreads into and out of the synovial fluid. Dispersal into the joints happens when plasma levels are upper than those in the synovial fluid, after which the progression reverses and synovial fluid levels are

**Table 5: Test characteristics**

Characteristics	Group A (n=40) diclofenac (%)	Group B (n=40) hydroxychloroquine (%)	p values
Age (mean±SEM)	51.66±2.17	50.27±1.36	0.1726
Female (n=64)	35	29	0.3428
Alcoholic	3 (3.75)	4 (5.00)	0.2217
Smoker	1 (1.25)	0 (0.00)	0.2916
ESR (mean±SEM) (before treatment)	37.6±4.12	35.8±2.76	0.2317
Pain control time	1.24±0.6 h	3.12±2.24 h	0.0496*
Time taken for remission of pain	2.56±0.3 h	7.44±1.16 h	0.0047*

\**p*<0.05 is considered significant at 95% confidence interval

Table 6: PCS and MCS

Groups	Group A			Group B			p value <sup>a</sup>
	Before	After (a)	p value	Before	After (a)	p value	
PCS	36.12±2.17	44.72±1.26	0.0927	36.82±1.17	54.17±2.26	0.0236*	0.0436*
MCS	31.16±2.47	39.16±0.97	0.0628	31.29±1.62	51.17±1.12	0.0059*	0.0061*

<sup>a</sup>Comparison of after treatment of Group A and Group B, \*p<0.05 is considered significant, PCS: Physical component score, MCS: Mental component score

Table 7: Treatment efficacy after 3 months depending on SF-12

Groups	Number of patients with improvement	Number of patients without improvement	Total
Group A	28	12	40
Group B	35*	5	40
Total	63	17	80

On performing  $\chi^2$ , Group B value was found to be 12.167 and p value was found to be 0.0396. p<0.05 is considered to be statistically significant at 95% confidence interval

Table 8: ADR reported in the study

ADR	Group A (n=40)	Group B (n=40)	p value
GI ulcers	12 (15.00)	2 (2.50)	0.0327
Nausea/vomiting	7 (8.75)	4 (5.00)	0.0926
Tinnitus	0	4 (5.00)	0.0927
Leucopenia	3 (3.75)	9 (11.25)	0.2716

ADR: Adverse drug reactions, GI: Gastric. p<0.05 is considered to be statistically significant at 95% confidence interval

higher than plasma levels. It is not known whether diffusion into the joint plays a role in the efficiency of diclofenac. However, it shows rapid onset of action when compared to hydroxychloroquine.

Gastric acid plays a tolerant role both in *Helicobacter pylori* and NSAID-induced ulcers. Thus proton-pump inhibitors are useful for primary and secondary ulcer prevention [12].

## CONCLUSION

Hydroxychloroquine offers a newer spectrum in the management of OA. Although it is slow acting, it has significantly increased the quality of patient as it can have a prolonged action. Hence, hydroxychloroquine can be used as a newer entity in the management of OA.

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