



RESEARCH ARTICLE

PHARMACOLOGY

EFFICACY OF CHLOROQUINE IN MANAGEMENT OF CHIKUNGUNYA: A PHASE IV CLINICAL TRIAL*Corresponding Author***DR. DILIP KUMAR RENAPURKAR**

**M.D. (Pharma) Private Practice Sanathnagar (Assistant Professor
Deccan College of Medical Science Hyderabad, Andhra Pradesh
India), Hyderabad India**

ABSTRACT***Back Ground***

Chloroquine in a new role for control and cure of Chikungunya

The aims of this study are

Primary objectives :-

1. To Evaluate efficacy of Chloroquine in treatment of Chikungunya
2. To Monitor Adverse Drugs reaction of Chloroquine.

Study Design and methods:

Severe epidemic of Chikungunya occurred in the year 2006 in city of Hyderabad and adjacent areas as well. The diagnosis of Chikungunya was difficult. All the cases presenting to a private practice numbering around 193 were put on Chloroquine 10 mgs / kg either injectable, per oral form or syrups. In addition to Chloroquine, patients were administered oral Paracetamol 500 mg, 4 times a day for 3 to 5 days.

Chloroquine given for one week initially like anti malarial regimen later on tapering dosages 250 mgs tablets orally. Pain was assessed by Visually analogue scale and adverse drug reaction monitored by Noranjo scale.

Interpretation

We can conclude that Chloroquine is very useful drug in the management of Chikungunya. It was found to be efficacious in management of severe arthritis pain as well as fever when combined with Paracetamol.



KEY WORDS

Immuno modulatory role, Chloroquine phosphate, Aedes Aegypti mosquito, Alpha viruses

INTRODUCTION

Chikungunya is a viral fever caused by an alpha virus. The role of vector for the spread of Chikungunya is played by Aedes aegypti mosquito. Aedes Aegypti is also a vector for Dengue hemorrhagic disease. Chikungunya disease was first detected and described in African continent by Marion Robinson and W.H.R. Lumsden in 1955 in Mekonde plateau near Tanganyika.

What are the trials published until now :

1. Chloroquine phosphate in the treatment of chronic chikungunya arthritis¹
2. Assessment of Invitro prophylactic and therapeutic efficacy of chloroquine against chikungunya virus in vero cells²

Chloroquine:

Chloroquine is conventionally used drug in clinical practice for the treatment of Malaria. It has specific role in Rheumatoid arthritis patients where it works as disease modifying anti rheumatic drug. It has been found to have a similar kind of immune-modulatory role in the management of Chikungunya. Chlorine atom attached to position 7 constitutes greatest anti malarial activity . The Toxicity of Chloroquine is reduced in form of hydroxyl Chloroquine and its analogues which are used for therapy of conditions other than malaria . This alkaloid concentrates itself in lysosomes and has anti inflammatory properties . Thus

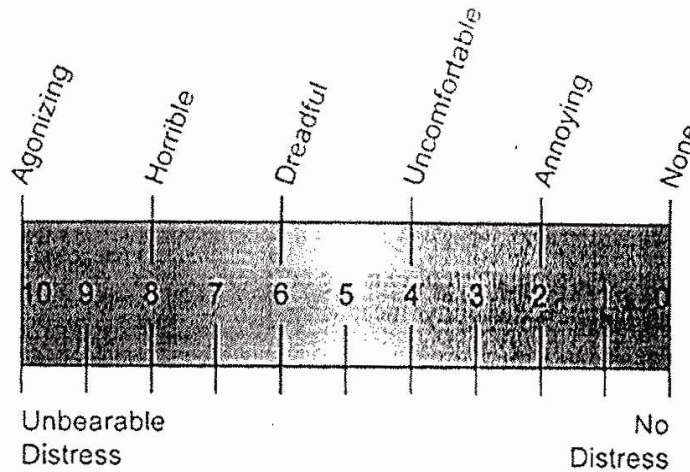
these compounds often with other agents have effects on Rheumatoid Arthritis , SLE Systemic Lupus erythematosus , Sarcoidosis photosensitivity diseases such as Porphyrea Cutanea Tarda⁷.

This study was carried out during epidemic of chikungunya in a private practice clinic set up. The recent outbreak of Chikungunya fever in the twin cities of Hyderabad and Secunderabad, India was declared by W.H.O in the month of December 2005. Currently there is no specific treatment protocol for Chikungunya. The purpose of this study was to prove the efficacy of Chloroquine in the management of Chikungunya.

During the Chikungunya epidemic outbreak in the month of June 2006, Chloroquine phosphate was administered to the patients diagnosed with the condition in the form of injectable/ per oral tablet/ syrup.

A total of 193 cases were seen during the period of 3 months from the month of June 2006 to August 2006, out of the 193 cases of Chikungunya 90 patients were males 103 females. All these cases were diagnosed on the basis of signs and symptoms associated with Chikungunya like fever, severe arthritis resulting in inability to ambulate. The improvement in the pain was studied using visual analogue scale while adverse events were studied by Noranjo algorithm scale⁵.

VISUAL ANALOGUE SCALE



Severe moderate mild

Every day 10mg per kg Chloroquine given for adults and 5 mg/kg for children. No Chloroquine injections below 5 years and precautionary use in children above 5 years of

age and below 10 years . During the fever period Paracetamol 2 gms per day was given for 3 to 5 days during the first 7 days.

Comparative Improvement in visual analogue scale

VAS	Day 0	Day 1	Day 2	Day 3
1	Mild n=94	Progressive Improvement 2.55 cm .	Progressive improvement	All the cases improved VAS NIL
2	Moderate N=55	7.5cm progressive Improvement	Progressive improvement	VAS Nil
3	Severe N=35	7.5 progressive improvement	Progressive improvement	Progressive improvement
4	7 patients at various Levels of pain	Lost to follow up		Presumed to be managed well.

.Another 7 days of administration of only chloroquine was continued for moderate to severe cases. Treatment completed after the

additional 7 days of Chloroquine administration in all the patients.

Morbidity was found to be reduced with Chloroquine tablets. Most of the cases demonstrated dramatic relief from pain and fever within 3 days of starting the Chloroquine course and rest of them in the next 7 days. All



the 193 patients diagnosed with Chikungunya were successfully managed with Chloroquine.

Safety of Chloroquine :

Safety of Chloroquine has been established since time immemorial in the use as an anti-malarial drug. Chloroquine phosphate is considered safe during pregnancy and in children. Safety of Chloroquine was studied by Norenjo scale where it stands at 1 to 4.

DISCUSSION AND CONCLUSIONS

Chloroquine Phosphate is one of the oldest drug in market with proven safety. Most important finding in this study is efficient management of Chikungunya which has high morbidity. It's immune-modulatory role has been proved by in vitro prophylactic and therapeutic efficacy of Chloroquine against Chikungunya virus in Vero cells².

Chloroquine Phosphate can be used in the treatment of Chikungunya. During the acute phase of first 3 days involving fever it can be combined with Paracetamol for 3-5 days and then only Chloroquine tablets could be continued for 7 days.

Chloroquine is the drug already in use, and well known not to have any adverse effects even when it is used up to 3 months in 250 mgs dosages in cases of rheumatoid arthritis.

The particular conclusions about this study is remarkable patient improvement with Chloroquine almost completely in most patients on VAS scale .

Chloroquine is already proved disease modifying anti-Rheumatoid arthritis drug . There are also studies which have assessed invitro prophylactic and therapeutic efficacy of chloroquine against chikungunya virus in vero cells² based on this I can conclude that there is a huge role for Chloroquine in the management of Chikungunya .

ADVERSE EVENTS

Adverse events can be studied by Naranjo Algorithm

Question:	Yes	No	Do not know
1. Are there previous conclusive reports on this reaction?	+1	0	0
2. Did adverse event appear after the expected	+2	1	0



(Naranjo C A, Busto U, Sellers E M et al (1981), A Method of Estimating the Probability of Adverse Drug Reaction. *Clinical Pharmacology and Therapy* 30: 239-245.)(5)

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