

Ribavirin therapy for Chikungunya arthritis

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Abstract

Background: Chikungunya is an acute viral infection presenting with a febrile episode and severe arthralgia, swelling of soft tissues, especially around the ankles. Many patients recover with nonspecific treatment of analgesics. Some patients continue to have subacute crippling arthritis in the legs affecting their mobility. This study was undertaken to see the effect of the antiviral drug Ribavirin in the clinical outcome of these patients.

Methodology: Ten patients who continued to have crippling lower limb pains and arthritis for at least two weeks after a febrile episode were taken up for the drug study. Ten similar patients during the same period were included as controls. In the study group Ribavirin was given at 200 mg twice a day for seven days. Both groups were followed up for four weeks

Results: All patients in the drug group reported improvement in the joint pains with six of them capable of walking freely. The soft tissue swelling also reduced in eight. In three patients the pain returned after mobilization. Seven patients continued not to receive analgesics after four weeks.

Conclusions: Ribavirin may have a direct antiviral property against Chikungunya leading to faster resolution of joint and soft tissue manifestations.

Key Words: Chikungunya, lower limb arthritis, Ribavirin, observational study.

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Introduction

Chikungunya is a viral fever transmitted to humans by the bite of the *Aedes Aegypti* mosquito. The virus belongs to the Genus Alpha virus, family *Togaviridae*. The disease was first described in 1955 by Marion Robinson and W H R Lumsden in the African subcontinent. The outbreak was in the year 1952 [1,2]. Since then, several cases have also been reported from the Asian subcontinent [3]. Recently there have been large outbreaks of Chikungunya in several districts of India in the last few months [4]. According to the World Health Organization (WHO), more than 1.25 million suspected cases have been reported from India up to October 2006 [5]. The clinical picture of the disease is high fever after a short incubation period with constitutional symptoms including headache, photophobia, etc. Migratory arthralgia of the small joints of the hand, wrist, feet and ankle are common. Rash may also appear. The fever disappears in two to three days. However several patients may have pain, stiffness, and swelling of the joints, especially in the lower limb around the ankles. This leads to considerable morbidity due to

the effects on the patient's mobility. The crippling pain can last several months [6]. There has been no specific treatment described for Chikungunya. Antipyretics and analgesics form the mainstay of treatment. In those patients who continue to have chronic joint pains, Chloroquine has been tried with some success [7]. This observational study was undertaken to determine the effect of the antiviral drug Ribavirin in the outcome of joint manifestations of Chikungunya. A randomized placebo controlled trial could not be undertaken since the disease disappeared from the country.

Materials and Methods

Ten patients who had severe arthralgia, lower limb swelling, pain and difficulty in walking after a febrile episode were taken up for the administration of Ribavirin. Ten similar patients during the same period were included as controls. Those patients who recovered spontaneously within two weeks after the febrile episode were excluded from the study. All critical patients and those with systemic disease were excluded from the study. Routine hematological and biochemical

investigations were conducted in the beginning and end of the study. CRP and IgM antibodies to Chikungunya were estimated in all the patients. Only patients with positive antibodies were included in the study. All the patients were followed up for a period of four weeks. An arthritis score was used to assess the joint involved, joint pain, joint tenderness and swelling in a scale of zero to five in the patients.

Similarly, an evaluation by the patient on a five-point scale was also undertaken. The patients were evaluated on a weekly basis for 4 weeks and called again after 8 weeks. In the study group all analgesics were stopped and Ribavirin in the dose of 200mg twice a day was given for seven days. The female patients were screened for pregnancy before administering the drug. The control group continued to receive analgesics as and when required. Although the drug is well established for other viral infections, approval of the ethics committee of the hospital was obtained since it is a new indication.

Results

In the study group out of the ten patients, five were males and five were females. Ages ranged from 27 to 74 years. Interval from the febrile episode was two weeks to two months. Three patients had leucopenia. In six patients the CRP was positive. In the control group, five were males and five were females. Ages ranged from 25 to 70. CRP was positive in five patients. In the study group all patients reported improvement in pain. Seven patients were able walk better. In eight patients there was reduction in joint and soft tissue swelling. In three patients the pain relapsed. At the end of four weeks, analgesics were discontinued in seven patients. Two patients complained of nausea and weakness. No other side effects were seen. Three patients were restarted on analgesics.

The results of both groups are shown in the Table 1.

Discussion

Although Chikungunya is a self-limiting viral disease with hardly any mortality, a considerable number of patients continue to have crippling joint pain in the lower limbs which affects their mobility. These patients continue to take analgesics for long periods of time with possible complications. The joint manifestations could also become chronic,

even lasting for years. Brighton reported the use of Chloroquine phosphate for twenty weeks with significant improvement in Chikungunya arthritis.

Table 1. Clinical Features and Outcomes in the patients studied.

	Study Group	Control Group
Total Number of Patients	10	10
Male	5	6
Female	5	4
Age Range	27 – 72	25 – 65
CRP +ve	6	4
Improvement in pain	10	10
Improvement in walking	7	3
Reduction in swelling	8	6
Relapse of pain	3	7
Patients free of analgesics	7	3

Ribavirin is a synthetic nucleoside analogue that inhibits a wide range of RNA and DNA viruses. The mechanism of action of Ribavirin is not completely defined and may be different for different groups of viruses. It has been used successfully in chronic Hepatitis C in association with interferon, respiratory syncytial virus, Lassa fever virus, and Hantaan virus [8,9,10]. This study was undertaken to determine whether antiviral treatment would make any difference in those patients who continue to have arthritis even after two weeks after the febrile episode. Ribavirin was chosen in view of its broad spectrum. Our preliminary observation shows a definite improvement in these patients. Since we had chosen patients in the subacute phase, some improvement could be attributed to the natural history. Briolant *et al.* have shown *in vitro* a combination of interferon alfa 2B and Ribavirin has a synergistic antiviral effect against Chikungunya virus¹¹.

Our study has several limitations: a) it involves only a small number of patients; b) it was not a planned study where the patients could be distributed randomly and compared with a group receiving placebo. This was not possible since the disease rapidly disappeared from the country. However, our observations may assist other centers in the world undertaking clinical trials of the drug.

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Conflict of interest: No conflict of interest is declared.