**Case Report**

J Vect Borne Dis 42, March 2005, pp 36–38

# *Tinospora cordifolia* as an adjuvant drug in the treatment of hyper-reactive malarious splenomegaly – case reports

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*Background & objectives:* The effect of aqueous extract of *Tinospora cordifolia*, an immunomodulator with antimalarial activity along with chloroquine was studied in the treatment of three cases of hyper-reactive malarious splenomegaly in District Hospital, Daltonganj town, Jharkhand, India. These cases were partial/slow responders to the conventional antimalarial drug chloroquine.

*Methods:* Aqueous extract of *T. cordifolia* (500 mg) was added to chloroquine (CQ) base (300 mg) weekly and CQ prophylaxis was observed up to six months. Improvement was gauzed by measuring spleen enlargement, Hb, serum IgM and well-being in three cases of hyper-reactive malarious splenomegaly.

*Results:* Addition of extract of *T. cordifolia* for the first six weeks to chloroquine showed regression of spleen by 37–50% after six weeks and 45–69% after six months from the start of treatment. Likewise decrease in IgM and increase in Hb as well as wellbeing (Karnofsky performance scale) were observed.

*Conclusion:* The results of the present study paves a new sight in the treatment of hyper-reactive malarious splenomegaly, however, large-scale trial is required to confirm the beneficial effect of *T. cordifolia* extract in combination with chloroquine.

**Key words** Antimalaria activity – hyper-reactive malarious splenomegaly – immunomodulator – *Tinospora cordifolia*

*Tinospora cordifolia*, a climbing shrub belonging to the family Menispermaceae is widely distributed throughout Indian subcontinent and China[1]. Aqueous extract of stem and root of the plant has been used therapeutically because of immunomodulation property as well as antimalarial and antileprotic activities[1,2]. The aqueous extract contains a number of chemical constituents—alkaloids, steroids, glycosides, polysaccharides, etc. The practice in Ayurveda—Indian System of Medicine is to prescribe decoction of stem of *Tinospora* with piper longam in malarial fever. It helps in reducing splenomegaly too. The alcoholic extract of the plant is prescribed in Ayurveda and Allopathy as an immune promotor. Hyper-reactive malarious splenomegaly (HMS) is thought to be the result of immunological dysfunction due to recurrent episodes of malaria. HMS is treated by chloroquine (CQ)/proguanil/pyrimethamine prophylaxis[3]. There is paucity of clinical trials to compare the efficacy of different antimalarial drugs in HMS. Duration of treatment in HMS is also not clear. Some view for lifelong prophylaxis, while others favour for more than a year. However, immunological abnormalities in tropical splenomegaly—gross increase in IgM, higher titres of IgM anti-

bodies against *Plasmodium vivax* and low circulating T-lymphocytes reverted towards normal after 9–26 months of weekly CQ prophylaxis[4]. Cases of fulminant HMS have been uncommonly reported and were treated with steroids and cytotoxic drugs[5].

Reports of three cases of HMS having defined criteria[6] (spleen size > 10 cm, IgM > 2 SD of local mean and response to antimalarial treatment) are presented. The ethical clearance was obtained from the Ethic Committee of District Hospital, Daltonganj. All three patients gave their free consent for the present study. All the three cases (case 1—45 yr male, case 2—25 yr female and case 3—50 yr male) were partial/slow respondent cases of HMS (spleen shrinkage rate was 15–20%) to CQ (Resochin, Bayer's India) 300 mg base weekly prophylaxis given for one year. All the three cases belonged to Daltonganj town (India) being endemic zone for vivax malaria. After dropping CQ for 2–3 months they developed fever (100–104°C) and haemolytic anaemia during April to June 2003. Clinical examination revealed no other observable cause of huge splenomegaly. Total and differential WBC counts were within normal range except low haemoglobin level. Malarial parasites were not found in peripheral blood smear, however, high titres of malarial antibodies against *P. vivax* were present. Raised serum bilirubin (mostly unconjugated) was estimated and direct coombs test was found negative. Urinalysis showed presence of haemoglobin. Deficiency of Glucose 6-phosphate dehydrogenase was not demonstrated. Liver function tests were normal with absence of viral markers. Aqueous extract of *Tinospora cordifolia* (Immumod, Wockhardt Ltd., India) 500 mg (tablet) bd daily for six weeks was added to CQ 300 mg base weekly. CQ prophylaxis was continued for six months. Improvement was gauzed by measuring spleen enlargement, Hb, serum IgM and wellbeing (Karnofsky performance scale[7]) at Day 0, 6 weeks and 6 months (Day 0 being the first day of Immumod administration) (Table 1). Fundus examination was done prior and after CQ administration. Immumod was found to be safe drug as it produced no side effects in these cases.

In case 1 spleen regression was found 50% at six weeks and 67% at six months, while case 2 had spleen regression by 50% after six weeks and 45% after 6 months. Case 3 had spleen regression 37 and 69% after six weeks and 6 months respectively. Increment of Hb, reduction in serum IgM and well-being were marked as shown in Table 1.

Three cases of HMS who were given one year CQ prophylaxis showed slow rather partial response on the basis of reduction in spleen size. Response of antimalarial drug in HMS has been termed as good response or partial/slow response if spleen shrinkage is >40% or between 15 and 30% respectively. These cases developed haemolytic episode with fever at one stage after dropping CQ prophylaxis. Episodes of haemolysis occur occasionally in HMS and appear to

**Table 1. Showing clinical and biochemical profile of the cases**

| Parameters studied | Case 1 | | | Case 2 | | | Case 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Day 0 | 6 wk | 6 mth | Day 0 | 6 wk | 6 mth | Day 0 | 6 wk | 6 mth |
| Spleen size (cm) | 12 | 6 | 4 | 10 | 5 | 4.5 | 16 | 12 | 4 |
| Hb (g/dl) | 10 | 12 | 13.6 | 8 | 9.6 | 10.2 | 4.8 | 6.5 | 10.5 |
| IgM (mg/dl) | 400 | 310 | 280 | 295 | 180 | 180 | 1755 | 750 | 300 |
| Well-being (%) | 70 | 90 | 90 | 80 | 90 | 90 | 60 | 80 | 90 |
| Bilirubin (mg/dl) | 2.4 | 0.6 | 0.8 | 2.3 | 0.8 | 0.8 | 1.8 | 1 | 0.6 |

be due to autoimmune, cold agglutinin mediated response triggered by non-patent parasitaemia[9]. Addition of *T. cordifolia* aqueous extract to the treatment of HMS for initial six weeks accelerated the well-being with subsidence of haemolytic state besides marked reduction in spleen size and serum IgM as well as rise in Hb in all the three cases. Its beneficial effect in HMS was perhaps shown due to its immunomodulatory effect as well as additive effect on antimalarial activity of CQ. This report, on a small number of cases, paves new insight in the treatment of HMS. However, trial on large number of cases is required to confirm its beneficial effect.

## Acknowledgement

Dr. U.S. Prasad, GAMS (Ayurveda) at Daltonganj is gratefully acknowledged for providing details of herbal products. Help rendered by M/s. Ranbaxy Laboratory, Mumbai, India in serum IgM estimations by nephelometry is also gratefully acknowledged. There is no funding for this study.

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