94.3% (66/70) males and all (47/47) females achieved final clinical response. All the patients in Efficacy Evaluable population (118) were compliant to treatment and hence the treatment compliance was 100%. During the study 28.6% (34/119) subjects reported at least one adverse effect (AE). Majority of the AEs were classified as mild, 16 AEs were of moderate severity, 2 were severe. During the study, 2 subjects (1.7%) reported AEs from Ear and Labyrinth Disorders, which included ear pruritus and hearing impaired.

Conclusion: Paromomycin 11 mg/kg, once a day, intramuscular injection, for 21days was found to be 96.6% effective, and safe. All patients were compliant with the treatment. This study thus provides evidence to introduce PMIM in government health facilities in rural areas of Bangladesh.

- RESERVOIRS
[1097]

O 110 - **DOMPERIDONE IS AN EFFECTIVE TREATMENT FOR MILD CASES (LEISHVET STAGE I) OF CANINE LEISHMANIOSIS: A DOUBLE BLIND PLACEBO CONTROLLED TRIAL**

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Keyword:canine leishmaniosis; domperidone; treatment

Abstract:

In European countries, treatment of seropositive dogs that are clinically healthy or present only very mild clinical signs (stage I in the Leishvet classification)1 poses a difficult challenge. Treating these animals with the licensed leishmanicidal drugs (meglumine antimoniate or miltefosine) raises ethical concerns because of the high numbers of dogs in this group in endemic areas and the possibility of developing resistances in the parasite. A considerable proportion of these dogs are able to control the infection by themselves and remain healthy while many others will not build up an adequate immune response and will inevitably develop the disease, if left untreated. There is therefore a need to develop and validate alternative treatments able to protect these dogs and reduce the risks associated to an extensive use of leishmanicidals in dogs.

Domperidone, an immune potentiating drug has demonstrated efficacy in the treatment and prevention of canine Leishmaniosis.2,3 The aim of the present clinical trial was to investigate if domperidone was safe and effective as treatment for dogs seropositive and with only minimal clinical signs.

Thirty-eight seropositive (1/400 to 1/600 in the Direct Agglutination Test, DAT) adult dogs of different breeds, with at least one clinical sign compatible with leishmaniosis, were randomly assigned to the treatment group (n=20) or to the placebo group (n=18). Treatment group received 0.5 mg/kg of domperidone, PO, during 30 days. Three and seven months later all dogs were blood tested (DAT) and clinically examined.

At the end of the study 59% of the dogs of the treatment group were seronegative, compared with 10% of dogs in the placebo group. The antibody titers at the end of the study were significantly lower in the treated group ($P<0.01$). Similarly, the clinical evolution of the dogs of both groups was different. In the treatment group only 4/20 dogs showed a clinical worsening, compared with 7/18 dogs in the placebo group ($P<0.01$). No side effects attributed to domperidone were observed.

In summary, the present results demonstrate that domperidone administered at 0.5mg/kg/24h during 30 days can be a safe and effective treatment for seropositive dogs with very mild clinical signs and can help to reduce the use of leishmanicidal drugs in canines.

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- CLINICAL LEISHMANIASIS

[139]

O 111 - **INCREASING FAILURE OF MILTEFOSINE IN THE TREATMENT OF KALA-AZAR IN NEPAL AND THE POTENTIAL ROLE OF PARASITE DRUG RESISTANCE, RE-INFECTION OR NON-COMPLIANCE**

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Keyword:nepal, kala azar, visceral leishmaniasis; miltefosine; relapse

Abstract:

Miltefosine, the only oral drug for visceral leishmaniasis, is currently the 1st line therapy in the VL elimination program of the Indian subcontinent. Given the paucity of anti-VL drugs and the looming threat of resistance, there is an obvious need for close monitoring of clinical efficacy of MIL. In a cohort study of 120 VL patients treated with MIL in Nepal, we monitored the clinical outcomes up to twelve months after completion of therapy and explored the potential role of drug compliance, parasite drug resistance and re-infection. The initial cure rate was 95.83% (95% C.I. ±3.58%) and relapse rate at six and twelve months was 10.83% (95% C.I. ± 5.56%) and 20.0% (95% C.I. ± 7.16%) respectively. No significant clinical risk factors of relapse apart from age < 12 years were found (IRR 2.43; 95% CI 1.09-5.42). Parasite fingerprints of pre-treatment and relapse bone marrow isolates within 8 patients were similar, suggesting that clinical relapses were not due to re-infection with a new strain. The median promastigote MIL-susceptibility (IC50) of isolates from definite cures compared with that of relapses was not statistically different. Moreover, MIL blood levels at the end of treatment were similar in cured and relapsed patients. Relapse in one- fifth of the MIL-treated patients as observed in our study is an alarming signal for the VL elimination campaign, urging for further review and cohort monitoring of late treatment outcomes.

- BIOCHEMISTRY, CHEMOTHERAPY, DRUG DEVELOPMENT AND DRUG-RESISTANCE

[1039]

O 112 - **FUNCTIONAL CHARACTERIZATION OF ANTIMONY TRANSPORT IN THREE NEW WORLD RESISTANT LEISHMANIA SPP.**

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Keyword:new world leishmania spp. ; antimony resistance; transport