Julia A Loos et al., J Bacteriol Parasitol 2016, 7:3 (Suppl)
http://dx.doi.org/10.4172/2155-9597.C1.020

Preventive and clinical efficacies of metformin against experimental cyst echinococcosis

Julia A Loos and **Andrea C Cumino**
National University of Mar del Plata, Argentina

Metformin (Met) is an antihyperglycemic and a potential anticancer agent which may exert its anti-proliferative effects, both indirectly through the systemic reduction of insulin levels and directly, *via* the induction of energetic stress, involving the inhibition of ATP production, the activation of AMP activated protein kinase (AMPK) and the inhibition of the target of rapamycin complex (TORC1). The drug shows good oral bioavailability (50-60%), is stable and not metabolized and its pharmacokinetics is regulated by transporters of the major facilitator superfamily (MFS). The aim of this study was to test the *in vitro* effect of Met alone or in combination with low concentrations of albendazole (ABZ) on Echinococcus granulosus larval stage and to report on their effects *in vivo* employing murine cyst echinococcosis infection model. Viable protoscoleces (PTS, N=3000) and metacestodes (MTC, N=20) were cultured *in vitro* in 199 medium and mortality was calculated daily. To determine the *in vivo* clinical and chemoprophylactic efficacies, mice were inoculated intraperitoneally with viable PTS and then treated once daily by intragastric administration for 60 days with the Met (50 mg kg-1 day-1) and ABZ (5 mg kg-1 day-1), separately and in combination (both Met at 50 mg kg-1 day-1 and ABZ at 50 mg kg-1 day-1). Next, the hydatid cysts collected from the peritoneal cavity of the animals were weighed and analyzed by scanning and transmission electron microscopy, determining also the Met intracyst concentration. Administration of Met to cultured PTS and MTC showed significant dose and time dependent killing effects and the combination of Met and ABZ-SO, (the main active metabolite of ABZ), had an synergistic effect from day 12 or 4 in PTS and MTC, respectively. RT-PCR analysis indicated expression of the five genes encoding for Echinococcus organic cation transporters in PTS and MTC. In Met treated MTC an overexpression of all studied genes was observed, except for Eg-slcD; while that in PTS no changes in the transcriptional expression level of these genes was detected, except for Eg-slcE. In the clinical efficacy study, the weight of hydatid cysts was significantly decreased upon treatment with each drug ($P<0.01$), but the decrease was more prominent in the group receiving the combined treatments than that with either drug alone ($p<0.05$). In the chemoprophylactic study statistical differences ($p<0.01$) were registered in the weight of the cysts obtained from untreated mice compared with mice treated with Met. In addition, Met concentration was estimated in cysts obtained from Met or Met plus ABZ treated mice. Drug concentration was 43% higher in samples from animals treated with both drugs (60±5 µg/cyst g) compared to those receiving Met alone (35±7 µg/cyst g). Our results indicate that Met has anti-echinococcal effects and its combination with ABZ has significant additive effects, therefore both drugs may improve the anti-parasitic therapy.

Biography

Julia A Loos is graduated in Biological Science (National University of Mar del Plata, 2011) and she is pursuing her PhD under the direction of Prof. Dr. Andrea Cumino. She has been serving as assistant teacher for subjects such as Histology, General Microbiology and Farmacology, that are part of the Biology and Biochemistry courses of study. She participates in several research projects on Parasitology and has published original articles. Currently, her research is focused on the study of intermediary metabolism and energy control in the larval stage of *Echinococcus* spp.

julialoos@hotmail.com

Notes: