29th ECCMID Amsterdam, Netherlands 13 – 16 April 2019

The congress of ESCMID

P0223 Toxicity reduction of amphotericin B and improvement its therapeutic effects against *Leishmania major* by a dendrimer-based novel nanoformulation

Tahereh Zadeh Mehrizi[1], Ali Khamesipour[2], Nariman Mosaffa[3], Mehdi Shafiee Ardestani[4], Mostafa Haji Molla Hoseini[3], Hasan Ebrahimi Shahmabadi[5], Amitis Ramezani*[1]

[1] Department of Clinical Research, Pasteur Institute of Iran, Tehran, Iran, [2] Center for Research & Training in Skin Diseases & Leprosy, Tehran University of Medical Sciences, Tehran, Iran, [3] Department of Medical Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [4] Department of Radiopharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran, [5] Department of Microbiology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Background: The clinical application of amphotericin B (A) is limited due to severe side effects and low water solubility. This study used Anionic Linear Globular Dendrimer (ALGD) as a carrier of amphotericin B for treatment of leishmania major infection.

Materials/methods: ALGD nanoparticles with negative charge were synthesized and amphotericin B was loaded into the nanoparticles for the first time. The formulation was characterized in terms of size, zeta potential, morphology and chemical structure by using AFM, DLS, FTIR and HNMR methods. The toxicity of formulation was measured in vitro by MTT assay. Moreover, the formulations efficacy was determined in vitro by measurement of its killing effects against promastigotes and amastigotes. Furthermore, in vivo toxicity of formulations was measured by using enzymatic evaluation, pathological studies and mortality rate. Finally, the in vivo efficacy was determined by measurement the lesion size, pathological effects, parasite burden and number.

Results: The results showed that loading of A into ALGD (AD) can increase the solubility rate of our nanodrug by 478 times. Furthermore this nanoformulation became non-toxic in vitro by 100% and AD20 µg/ml showed the inhibition effects of 65% against promastigotes and amastigotes. Additionally, AD50 mg/kg was nontoxic without any tissue side effects and mortality rate, whereas A50 mg/kg showed tissue toxicity with 50% mortality rate. The toxicity was measured using pathological studies and enzymatic evaluation. The results of lesion size measurement in treatment of parasite infected mice confirmed by pathological effects in which the wound was recovered in a large extent. Moreover, the results of parasite burden were confirmed by measurement of parasite number in which AD50 mg/kg significantly inhibited leishmania major parasite by 65% which was as potent as glucantime (table 1).

Conclusions: Overall, the consistency between our in vitro and in vivo findings suggested amphotericin B loaded into ALGD (AD50 mg/kg) can be used as a promising candidate in decreasing A side effects in treatment of leishmaniasis.