

Therapeutic perspective of *Leishmania* Research: An Overview

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ABSTRACT

Leishmaniasis is a severe complex disease caused by *Leishmania* species, a protozoan parasite affecting the host of neglected rural areas mainly. Despite of being considered as neglected tropical disease which affects the antigen presenting cell of host organism, it has not been eradicated completely. Most of the cases were found to be related with increased drug cytotoxicity, high cost, less effectiveness etc. The present paper deals with recent advancement and therapeutic perspective in this regard. In addition to this immune therapy has also been advocated which might be safer and promising. The present study is based on different aspects of leishmaniasis in general and visceral leishmaniasis in particular in Saharsa district of Bihar.

Key Words :- Leishmaniasis, disease, visceral leishmaniasis, Protozoa, Bihar

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INTRODUCTION

Leishmaniasis has been recorded as the oldest protozoan infectious disease in the vast Indian sub continent caused by species of *Leishmania*, as Visceral leishmaniasis by *Leishmania donovani* and transmitted by bite of female sand fly, *Phlebotomus argentipes* affecting mostly poor mass of people due to their neglected life styles. The most severe form of disease has been recorded as Kala azar or black sickness. In India, Bihar in general and North Bihar in particular has been found to be most severely affected since 1950s and to see its fatal nature, eradication program was launched along with malaria eradication since that time but the large scale epidemic was yet recorded in 2007. World health organization also took step in this regard and started program for early diagnosis, vector control and effective treatment which finally resulted establishment of Kala-azar management information system. No doubt, the disease has been under control but Koshi division is still the alarming zone due to lack of awareness, flood and

insufficient basic amenities. In the course of study it was found that public health system should be self sufficient to anticipate and detect such risk factors to minimize the outbreak of leishmaniasis. A report of WHO (2014) says, "It has been estimated that the disease is prevalent in around 98 countries, around 4 to 12 million peoples across the globe with 2 million new cases registered each year and causing 20 to 50 thousand death annually. Despite of its fatal nature and global prevalence, this disease has not been given priority and still considered as neglected tropical disease because this disease has been found to be common in socio-economically weak people with lack of basic amenities. Sudden outbreak and the spread of the disease is associated with the changes in environmental conditions which is making more prone ambience for the growth of sand-fly vector, while the emigration of the people into the endemic areas are increasing the risk of mass individuals (Falcao *et al.*, 2018). Among different

forms of leishmaniasis, visceral leishmaniasis is the most fatal one affecting visceral organs. However, modern medical science has developed therapies but most of them are related with increased cytotoxicity showing increased drug resistance problems. Therefore, a serious and effective step is needed in this regard for complete eradication of this disease.

The present work is based on field survey and data collection in the Saharsa district of Bihar state. The district occupies 1,1687 sq. km area being surrounded by river Koshi in the west lying at 25°53' North latitude and 86°36' East longitude. The common poor mass of people have to face different kinds of natural disasters here, out of which, flood is the most important one which plays vital role in occurrence of such kinds of epidemics.

Therapeutic Approach & Major Treatments

The modern medical science has developed so many medicines for treatment of different kinds of leishmaniasis but they are out of reach of poor people due to high cost value. In addition to this, drugs of visceral leishmaniasis develop or increase drug resistance power of the causal organisms. The available remedy includes therapeutic approach, vaccination and immunotherapy. At present, the remedy or therapies to reduce the risk of disease includes the anti-fungal drugs, anti-protozoal drugs, antibiotics etc.

Antiprotozoan Agents & Antibiotics

This area of medicine includes drugs being efficient in killing parasites by suppressing or inhibiting their functions or by binding its cellular components. One of the most promising drugs which suppresses the functions and growth of protozoan includes miltefosine, sold under the commercial name of Miltef or Impavido, used against all kinds of leishmaniasis including visceral leishmaniasis. This is the drug which interferes with the functions of membrane lipids, being effective to suppress protozoal action by affecting membrane integrity and destroying the mitochondrial cytochrome c oxidase activity, which results apoptosis (Villa Pulgarin *et al.*, 2017).

The second medicine, pentamidine is an antibiotic which inhibits the growth of Leishmania by oxidative phosphorylation; another one is Fluconazole which is an anti-fungal agent blocking ergosterol and inhibiting the function of cytochrome enzyme. However, this is used against cutaneous leishmaniasis.

Pentavalent Antimonials

This part of drug includes antimonial drug as sodium stibogluconate sold under the commercial name of pentostam which, on long term therapy act by inhibiting the nucleotide metabolism of the parasite. This type of drug, when used with other ones has been supposed with lower chance of resistance and toxicity.

Systemic antifungal agent

The widely used antifungal drug against cutaneous leishmaniasis is the amphotericin B, being used in liposomal formulation with commercial name, Ambisome. It results lysis of cells after binding with the membranes. The low dose of tamoxifen along this antifungal agent increases the efficacy of action.

Vaccination

Because of frequent change in the surface antigen of protozoan, no effective vaccines have been available yet. This is the matter of great challenge in this regard, but as per as the vaccination approach is concerned, studies have shown the effectiveness of various forms of vaccination approach which includes the use of whole killed parasite, live-attenuated parasite and recombinant surface antigen and ligands which can be promising against disease progression and onset.

Development of Immunotherapy

Formulation of immune system to mound protective immunity is the recent trends in therapeutic approach widely known as immunotherapy. The therapeutic strategies include modulation of any components of immune system through activation of receptors, transcription factors, cytokines and chemokines gradients or elevated antimicrobial molecules which ultimately give rise to protective host response either self-

sufficient for the killing of the parasite or help to increase the efficacy of the anti-leishmanial drugs. Based on the recent advancement in the potential immunotherapeutic factors, the strategies of immunotherapy can be classified into activation of pattern recognition receptors and Induction of Cytokines response.

Activation of pattern recognition receptors are the protein receptors which include dendrite cells, natural killer T – cells, macrophages etc. which are responsible for sensing the pattern associated with molecules of the microbial origin and for sending signals for the activation of immune response. Induction of cytokines response is the second one. Cytokines are micro proteins which are secreted by the cells of immune system helping in the maintenance of the immune function by activation transcription factors, by polarizing T cells and / or by enhancing the generation of anti-microbial molecules. It has been found that application of recombinant lipophosphoglycan 3, a leishmanial derived molecule plays very important role in successful eradication of leishmaniasis. It has also been found that direct IFN γ therapy increases the therapeutic effects of visceral leishmaniasis. Therefore, it can be said that modulation of immune system is the important and the most effective part to fight against different forms of leishmaniasis in more and more natural and promising way.

CONCLUSION

Despite of being tropical neglected disease, leishmaniasis has been proven to be fatal not only in the state of Bihar but also at country or global level due to continuous emigration and anthropogenic activities. The major aspect that should always be kept in mind is that safety measures should have lower toxicity and high effectiveness as well as affordable for the common poor mass of people. The modulation of immunotherapy has been advocated here for the highest level of effectiveness. There is need of awareness also because in most of the localities, the affected persons have been found to be socially backward and unprivileged ones. Therefore recent

advancement in the therapeutic approach through monoclonal antibody-mediated selectivity in the target of leishmaniasis, and the use of immunotherapy parallel to the available conventional medicine for their better affectivity is proven to be worthy and a solution for the future encounter of the resistance.

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