

Beta-tubulin Isotype 1 Conferred Benzimidazole-resistance in Lymphatic Filariasis: an Explanation by Molecular Concern

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The lymphatic filariasis is an important lymphatic disease. It is the well-known lymphatic vessel disorder due to infection by a blood parasitic pathogen. The nematode parasite transmitted by mosquito is the cause of filariasis which can further result in severe disability in chronic infected cases. The filariasis is accepted as an important but forgotten tropical mosquito borne infection. The disease can be chronic and result in permanent disability, the elephantiasis. At present, this disease is still endemic in several tropical regions around the world. The management of filariasis can be by using antiparasitic drug. The Albendazole, anthelmintic benzimidazole (BZ) is generally used concomitant with diethylcarbamazine, in lymphatic filariasis management. Schwab et al. mentioned that "The Global Program for the Elimination of Lymphatic Filariasis intends to achieve its aims through yearly mass treatments with BZ combined with ivermectin (IVM) or diethylcarbamazine (DEC) [1]."

However, the resistance to BZ can be observed in clinical practice. The role of genetic polymorphism underlying the BZ resistance is of interest. There are some reports mentioning for some genetic polymorphisms of the parasite that can contribute to resistance to NZ. The mutation that results in replacement of phenylalanine (Phe) with tyrosine (Tyr) at position 200 of beta-tubulin isotype 1 is reported to be related to resistance to BZ [2-3]. As noted by Hoti et al. monitoring of this point genetic variant is suggested for monitoring of drug resistance of filariasis in endemic area [2]. The observed pattern of the mutation in each setting can refer to the drug resistance epidemiology in each specific area and can also a predictor for the success of treatment. The available PCR tool can be applied for such investigation of the mutation that can confer to the BZ resistance of the filarial pathogen [3]. Cobo concludes that "widespread of resistance to BZ is present because specific mutations in the gene encoding β -tubulin have been associated with drug resistance [4]."

The mechanism conferring to the resistance is very interesting. Here, the author used the quantum molecular approach for explanation for the observed resistance due to the mentioned mutation. Briefly, when the mentioned mutation, 200 Phe \rightarrow Tyr occurs, the molecular change from naïve molecule of beta-tubulin isotype 1 can be expected. The quantum calculation for the molecular weight change can be done and the derived change magnitude is 16 Da per mol. As described in previous similar studies on quantum molecular estimation for the genetic variant change in other disorders [5-8], the change in the present scenario of beta-tubulin isotype 1 can also affect the final pharmaco-biological process between BZ drug and filarial parasite. The increased molecular weight can imply more required molecular reaction energy between drug and parasite. This can further results in increased difficulty in successful drug pharmacological action. Hence, the mentioned 200 Phe \rightarrow Tyr mutation of beta-tubulin isotype 1 can pose resistance property to BZ. This short study can well clarify the myth about the resistance to BZ of tropical filarial parasite, which is still the problem in management of filariasis at present [9].

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Received August 03, 2017; Accepted August 14, 2017; Published August 24, 2017

Citation: Wiwanitkit V (2017) Beta-tubulin Isotype 1 Conferred Benzimidazole-resistance in Lymphatic Filariasis: an Explanation by Molecular Concern. *J Blood Lymph* 7: e123. doi: 10.4172/2165-7831.1000e123

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