

THERAPEUTICS OF HANSENIASIS - STATE OF THE ART

EDITORIAL

When the first results of PROMIN were presented by Faget in 1941, the leprosy world thought that the problem of hanseniasis was overcome. However, the limitations of sulfone were soon evident, ie. the long period necessary to achieve bacteriological negativation of contagious cases, unsatisfactory response in some patients and relapse after discontinuing the drug or even the treatment after clinical cure.

Floch, in 1947, was the first author to draw attention to the possibility of sulfone resistance. Souza Lima and Arantes in 1963 presented some cases of the Sanatório Pirapitinguy with longterm treatment and that still had active disease. At that time, there were some efforts towards the use of more than one drug, the long acting sulphonamide, vadrini, and thiambutosine.

In 1964 Petit and Rees presented experimental evidence of HD bacilli resistantes to sulfone. Although initially assumed as not frequent, soon it proved to be a major problem in areas of high prevalence of the disease.

PROMIN and other derivatives of sulf one were given daily for 20 or 45 days followed by a rest period of 10 to 15 days. In many places the drug was not administrated on sundays. Some authors suggested to start treatment with low doses with progressive increase in order to prevent ENL. During reactions the drug was discontinued. When Shepard established the minimal inhibitory concentration of sulfone through his research in mouse foot pad (1 mg/daily), lower doses were used in many patients. DADDS (diacetyl, diamino, diphenylsulfone) injected Intramuscularly each

75 days produced blood levels of sulf one of 5 mg/ daily and was administrated as monotherapy in large populations, including in Brazil. All these issues and the lack of cooperation of patients in regular drug taking due to the longtime of treatment led to the progressive increase of drug resistance. Besides secondary resistance, many patients are developing primary resistance. Resistance to other drugs such as rifampin and ethionamide has been reported, probably due to its use as monotherapy.

This situation led WHO to recommend new drug regimens based on rifampin, clofazimine and sulfone. All three drugs should be used in multibacillary cases (virchowian and borderline) and sulfone plus rifampin in the paucibacillary cases (tuberculoid and indeterminated). In multibacillary, rifampin, due to its strong bactericidal action, would destroy the small bacillary population of mutants resistant to clofazimine and sulfone and these two drugs would act to destroy the mutants resistant to rifampin in a not well determined period of time. In paucibacillary cases, rifampin would be the active drug, should the patient be infected with primary sulfone resistant bacilli.

An important fact is that rifampin taken monthly has the same effect as administered daily. This led these regimens to be less expensive and to the possibility of supervised drug administration. Finally, with multidrugtherapy the treatment could be discontinued after 6 months in paucibacillary cases and after bacteriological negativation or even after 2 years of treatment for the multibacillary.

This increased the compliance of patients to treatment once they knew they would not be taking drugs for life anymore. Furthermore, to start the new regimens health services could rearrange their organization leading to a better understanding among health personnel and improved care to patients, particularly concerning prevention of deformities.

Multidrug regimens are spreading all over the world and thousand of patients have already finished their treatment course. Their cooperation has been satisfactory and, up to now, only a few cases of relapse have been reported. There is no doubt that the WHO recommended MDT is the best choice now available for the treatment of Hansen's disease. However, it is not the ideal regimen mainly because only one drug is bactericidal (rifampin). On the other hand, there are some new bactericidal drugs being tested in patients, as ofloxacin, pefloxacin, minocyclin and claritromycin. These drugs are promissory and should take part in the MDT regimens in the near future.

Nowadays, we believe that the majority of

bacilli are destroyed at the beginning of the treatment. In fact, many centers are following up patients that discontinued drug taking while bacilloscopy was still positive. The supposition is that the bacilli are actually killed but the removal of debris occurs slowly due to the need of cellular immunity which is depressed or even not present in these patients. These debris would maintain an antigenic load that has the ability to develop immunological manifestations such as ENL which appear independently of treatment.

We conclude that even a combined drug treatment with high bactericidal drugs would not prevent the development of reactions and that the problem of slow decrease of bacterial index would still exist. Therefore, it is of utmost importance to concentrate efforts in the search for immunomodulators and for the development of a vaccine that would convert this picture to a better immunological condition of the patient.

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