LEADING PHARMACEUTICALS AND MISLEADING PROMOTION

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One of the important factor for the worsening control of tuberculosis in Pakistan and the emergence of Multi-Drug Resistant Tuberculosis (MDR-TB) is the inappropriate prescription by the treating medical practitioners. This includes inadequate doses and inappropriate combination of anti-TB drugs. Poor patient compliance has been a serious problem even with proper and standard prescriptions. WHO and IUATLD recommend that the only answer to the rapidly growing problem of tuberculosis is the adoption of a strategy called Directly Observed Treatment Short Course (DOTS). In this strategy all the TB patients are provided with standard anti-TB treatment free of cost and under direct supervision of a trained health worker. In the absence of a well organzsed National TB Control Program (NTP), while it is impossible to implement, better prescription by the attending doctors is one area where improvements can be made and better outcome can be achieved. This could only be possible through proper education and training of hospital and community Physicians so that they could provide treatment according to the current standards. WHO / IUATLD has set out guidelines for the management of tuberculosis which are endorsed by the Pakistan Chest Society, as well as National TB Control Program (I,2). According to these guidelines, patients of Tuberculosis are placed into four categories. Different combinations of Anti-TB drugs are recommended for each category. One of the most important aims of these guidelines is the judicial use of rifamicin, protecting it from being misused and therefor preventing the acquired resistance against this most important anti-TB drug.

While Pakistan Chest Society has been enthusiastically advocating the adoption of these guidelines by all the doctors treating tuberculosis, its voice can only go up to so far. All the leading pharmaceutical companion which are particularly involved in the manufacturing of Anti-TB drugs, have a well organized marketing network and have access to all most every doctor In the community. Pharmaceutical companies through out the world play a major role in the academic activities and education of hospital and community doctors. Through their help, latest recommendations and TB guidelines can be relayed to all the physicians involved in the treatment of tuberculosis. However, I have regrets to say that at least for the promotion of current WHO / IUATLD guidelines for the management of Tuberculosis, every single leading pharmaceutical company has failed to play their expected role. None of the leading manufacturer of the Anti-TB drugs has included these guidelines in their promotional literature and their medical representative are in fact promoting conflicting and potentially dangerous information through printed material as well as verbal communication. Unfortunately, the Pakistan Chest Society and National TB Control Program have so far been unable to establish a system in which they could educate every community physician regarding the current TB guidelines.

Consequently, the influence of pharmaceutical marketing has been unchecked and their promotional literature remain highly misleading. No single set of Anti-TB drug combination is fit for every patient of Tuberculosis. As an example, I would quote two major companies who promote the combination of Rifampicin, Isoniazid and Pyrazinamide for the first two months (Intensive phase). According to the WHO / IUATLD guidelines, this combination is only recommended for category – 3 patients which include children, extra pulmonary non serious tuberculosis

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and limited disease pulmonary tuberculosis which is sputum smear negative. Majority of our TB patient have extensive pulmonary parenchymal disease at presentation. They fall into category-1, for which the guideline recommend the use of four drugs for the intensive phase i.e. Rifampicin, INH, Ethambutol and Pyrazmimide. At the end of 2 months if they are sputum smear negative then the maintenance phase should be with two drugs excluding rifampicin i.e. Ethambutol + INH or Thiacetazone + INH. A vast majority of our patients never complete a full course of anti-TB treatment. In a well organised TB control programme run by Italian Cooperation for Development in NWFP region, only 23.3% patients completed the treatment (3). The defaulters either present with relapse or persistently active tuberculosis. According to the guidelines, they fall into category-2 for which the active phase of treatment should be started with 5 drugs i.e. Rifampicin + INH+ Ethambutol + Pyrazinamide + Streptomycin. Streptomycin is stopped after 2 months and Pyrazinamide after 3 months. Rest of the 3 drugs are continued for the maintenance phase. None of the pharmaceutical company mentions these guidelines. Not every TB patient needs four drugs for the intensive phase (Rifampicin, INH, Ethambutol and Pyrazmimide) or three drugs for the continuation phase (Rifampicin, INH, Ethambutol) as recommended pharmaceuticals. The most dangerous of all the suggestions marketed by the leading TB drugs manufacturers is the use of INH + Rifampicin for the maintenance phase. At least two studies of anti-TB drug sensitivity in Pakistan have shown acquired resistance against INH to be around 55 to 57% (4.5)). This means that up to 57% of patients using INH + Rifampicin are in fact using Rifampicin alone and therefore, likely to develop resistance against it. This practice must be stopped at all cost and Rifampicin should only be used with at least two other drugs to prevent acquired resistance against it. Combination of Rifampicin, INH and Ethambutol is used in the maintenance phase only in category – 2 patients which includes multiple defaulters and TB relapse cases or category 1 & 3 patients who remain sputum smear + ve after 5 months of treatment.

Resistance against Rifampicin is a serious matter and pharmaceutical industry should take serious and prompt action. All manufacturers of anti-TB drugs should adopt WHO / IUATLD guidelines for the promotion of their drugs. They should take every measure to protect Rifampicin. Another suggestion would be to stop manufacturing (only Rifampicin) tablets to avoid monotherapy. It will be a great help if such pharmaceuticals join hands with Pakistan Chest Society and the National TB Control Program for the promotion and adoption of DOTS strategy which can not be implemented by individual doctors and patients. In the mean time, we all must try to convey the right message across the medical community for the proper prescription of anti-TB drugs. The misleading information by the leading pharmaceuticals has to be stopped.

TB category	TB patients	Intensive Phase	Continuation Phase
I	New smear +ve PTB New smear -ve PTB with extensive parenchymal disease New cases of serious extra pulm. TB e.g. meningitis, spinal TB	2 months RHEZ	6 months HE or HT
II	Sputum smear +ve relapse Treatment failure Treatment after interruption Multiple defaults	2 months RHEZ + S 1 month more RHEZ	5 months RHE
III	New smear -ve PTB with limited disease New non-serious form of extrapulm. TB Childhood TB	2 months RHZ	6 months HE or HT
IV	Chronic cases, still sputum smear +ve after supervised category II treatment	Refer to the regional specialized centers.	

WHO / IUATLD guidelines for TB patients categories and treatment.

R = rifampicin, H = INH, E = ethambutol, Z = pyrazinamide, S = streptomycin, T = thiacetazone. All drugs to be given according to the body weight.

THIACETAZONE	2.5	mg / kg / day
INH	5	mg / kg / day
	(double in young children)	
RIFAMPICIN	10	mg / kg / day
	(double in young children)	
ETHAMBUTOL	15	mg / kg / day
STREPTOMYCIN	15	mg / kg / day
PYRAZINAMIDE	30	mg / kg / day

REFERENCES

Treatment of Tuberculosis: Guideline for National Programmes. WHO/TB/1997.

2. National Guidelines for Tuberculosis Control In Pakistan. Directorate of Tuberculosis Control, Federal Ministry of Health, Pakistan 1995.

3 Italian Cooperation for Development (ICD). TB control programme in NWFP. Annual report 1994;12.

4. Safi MI, Macor G, Habibi GQ. Proceedings of First Biennial Conference on chest diseases and tuberculosis, Peshawar. Primary and acquired resistance to TB drugs in Pakistani patients in NWFP. March 1994:55.

5. Aziz A, Siddiqui SH, Aziz K, Ishaq M. Drug Resistance in mycobacterium tuberculosis isolated from treated patients in Pakistan. Tubercle 1989;70:45-52.