

## ACQUIRED DRUG RESISTANCE TO INH IN PULMONARY TUBERCULOSIS

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### ABSTRACT

A prospective study of 52 culture positive patients who were admitted consecutively and were having definite history of previous anti-tuberculous therapy was performed. Out of total patients 39 (75%) were found to be resistant to INH singly or in combination with other anti-tuberculous drugs.

### INTRODUCTION

Isoniazid (INH), isonicotinic acid hydrazine is the most important anti tuberculous drug. It was synthesized in 1912 but its use in the treatment of tuberculosis was first reported by Selikoff and Robitzek in 1952<sup>1</sup>. It has no activity against non mycobacterial pathogens and among atypical mycobacteria only M-Kansasii is usually sensitive to this drug<sup>2</sup>. It is bacteriostatic for resting bacilli but is bactericidal rapidly for dividing tubercle bacilli. It has most of the properties of an ideal drug, being highly effective against tubercle bacilli, rapid absorption from the gastrointestinal tract with no major toxicity and low in cost.

In vitro, INH inhibits most tubercle bacilli in a concentration of 0.2 UG/ml or less. Resistant mutants occur in susceptible Mycobacterial population with a frequency of about 1 in 10<sup>6</sup>. Since tuberculous lesions often contain more than 10<sup>7</sup> Tubercle bacilli, resistant mutants could be readily selected out if the patient is receiving only INH<sup>3</sup>.

### PATIENTS AND METHODS

52 culture positive patients, varying from 15-80 years of age who were admitted consecutively were studied. All the patients had definite history of previous anti tuberculous therapy including INH before admission.

Following investigations were performed.

1. Blood examination for Hb, TLC, DLC, ESR.
2. Tuberculin test (STU).
3. Sputum examination for AFB for 3 consecutive days.
4. Sputum for AFB culture and sensitivity.
5. Chest X Ray PA view.

Sputum was examined by concentration method and culture was inoculated on Lowenstein Jensen tension medium without potato – Drug sensitivity tests were proposed on cultures obtained on L-J medium by proportion method and the concentration of drug was 0.2 ug / ml<sup>4</sup>.

### RESULTS

Of the 52 patients who had a definite history of previous chemotherapy including INH, 33 patients (63%) were resistant to one or more drugs tested. The total number of patients resistant to only INH were 22 (42%). The total number of patients who were resistant either to only INH or INH and another drug was 39 (75%). Double drug resistance to INH and streptomycin occurred in 12 (23%) while triple drug resistance to INH + streptomycin + Ethambutol was found in 2 patients (3.8%) while 3(5.7%) were resistant to INH + Streptomycin + Ethambutol + Rifampicin.

### DISCUSSION

In Pakistan Tuberculosis is a major health problem and is the fourth cause of death<sup>5</sup>.

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Like other developing countries the incidence of acquired drug resistance to INH is quite high – It varies greatly from place to place and year to year. Gilani and Khan<sup>6</sup> noted 27.06% in one study while 71-1% in another study. In Peshawar region Muhammad Zahid found 44% and in another study in the same city it was reported 56.97%<sup>7</sup>. In multiculture study completed at the Pakistan Medical Research Council Lahore, Raja and Colleagues<sup>8</sup> noted acquired drug resistance to INH in 41-9% cases. Acquired drug resistance to INH is high in most of the countries, 62% in Hong Kong<sup>9</sup>, 33-7% in Japan<sup>10</sup>, 57% in Korea<sup>11</sup>, 28% in Kenya<sup>12</sup>. In UK during 1956-1959<sup>13</sup> it varies from 37 to 50% while during 1956 to 1961 overall resistance was noted about 62%. In USA during 1975-1982<sup>15</sup>, 25.9% were resistant to INH. In Vietnam the rate of acquired INH resistance was 72%. Isoniazid is the cheapest and most commonly used drug. Most interest has been devoted to the rate of isoniazid resistance. Since for many years this has been the main stay of treatment and problem of tuberculosis.

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