LETTER TO THE EDITOR

SERUM CONCENTRATION OF ISONIAZID FOLLOWING ADMINISTRATION OF THE DRUG ALONE AND IN COMBINATION WITH RIFAMPICIN IN PATIENTS OF PULMONARY TUBERCULOSIS

Sir,

(Received on August 2, 1985)

Combination of rifampicin and isoniazid in an effective and widely used treatment for tuberculosis (4). Rifampicin being a potent enzyme inducer influences kinetics of many drugs administered simultaneously (1). The anticoagulant effect of acenocoumarol (7) and warfarin sodium (10), hypnotic effect of phenobarbitone sodium (3), contraceptive effect of oral contraceptives (8), antidiabetic effect of tolbutamide (11), anticonvulsant effect of methadone (5) and antiarrhythmic effect of quinidine (2) are reduced and this requires adjustment of their dosage when rifampicin must be given concurrently.

Isoniazid is metabolised by the process of acetylation in liver. It was thought worthwhile to study the effect of rifampicin on the serum levels of isoniazid. The study was planned as within subject comparison of serum levels of isoniziad administered alone and in combination with rifampicin.

A total of 10 patients suffering from pulmonary tuberculosis, with liver and renal functions within normal limits, were selected from Tuberculosis and Chest outpatients Department of J. N. Medical College Hospital, A.M.U., Aligarh. These included 5 males and 5 females with a mean age of 31.5 year (18-51 years) and a mean weight of 39.0 *kg* (35-44 *kg*). The patients were not given any drug for seven days before the study. Acetylation status of all the patients was determined by a method described by Schroder (9) to designate a patient as a slow or rapid acetylator.

After an overnight fast patients were administered 300 *mg* isoniazid orally with 200 *ml* of water at 8 a.m. Food was withheld for further 2 hr. Venous blood samples

were collected at 2, 4 and 6 hr after isoniazid administration. Serum was separated and stored in glass stoppered bottle at 5°C till quantitative estimation of isoniazid, which was done within 2 days of sample collection. Isoniazid was estimated in serum by Spectrophotometric method (6).

After a drug free interval of 3 days, same patients were administered a combination of isoniazid (300 *mg*) and rifampicin (450 *mg*) after an overnight fast orally on empty stomach with 200 *ml* of water at 8 a.m. Samples of venous blood were collected, serum separated and stored as described above.

Serum concentrations of isoniazid when the drug was administered alone and in combination with rifampicin are presented in Table I.

TABLE I : Serum concentrations of isoniazid (*μg/ml*; mean ±SEM) at various times when the drug was administered alone and in combination with rifampicin.

	No. of patients	*Mean serum Isoniazid levels (μg/ml) ± SEM*		
		2 hr	*4 hr*	*6 hr*
Isoniazid alone (10)				
Slow inactivators	(6)	4.2±0.171	2.96±0.245	1.73±0.11
Rapid inactivators	(4)	4.25±0.33	1.9±0.173	0.9±0.1
Isoniazid+rifampicin (10)				
Slow inactivators	(6)	4.3±0.177	2.93±0.217	1.66±0.08
Rapid inactivators	(4)	3.95±2.287	2.15±0.15	1.07±0.11
P = Slow inactivators		>0.1	>0.1	>0.1
Rapid inactivators		>0.1	>0.1	>0.1

The serum levels of isoniazid administered alone were not significantly different when the drug was administered simultaneously with rifampicin (Table I). This was true whether the patients were slow or rapid in-activators of isoniazid. It seem that a single dose of rifampicin does not influence absorption, metabolism or elimination of isoniazid.

ACKNOWLEDGEMENTS

Grateful acknowledgement is made to Indian Council of Medical Research, New Delhi and M/s Pfizer Laboratories for supplying isoniazid powder.

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