Effect of Activated Charcoal on Rifampicin Absorption in Man

Orisakwe, O. E., C. E. Dioka, A. N. Okpogba, C. N. Orish, and S. I. Ofoefule

College of Health Sciences, Nnamdi Azikiwe University Nnewi Campus, Anambra State, Nigeria
Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, Nigeria

(Received January 10, 1995; Accepted August 25, 1995)

The effect of activated charcoal (AC) on rifampicin excretion was investigated in six healthy volunteers. On three occasions, at weekly intervals, each subject received a 600mg rifampicin with 350ml of water; b-1c one and two weeks later, 600mg of rifampicin plus 7.5 and 15g AC, respectively, in 350ml of water as a charcoal slurry. Urinary levels of rifampicin were measured form 1-36 hr after ingestion. Treatment with AC led to 1.2 per cent urinary recovery of rifampicin; decreased excretion reta; and a much lower plateau indicative of reduced absorption.

(Key words: activated charcoal, rifampicin absorption)

INTRODUCTION

Activated charcoal (AC) is an adsorbent with a well-known ability to reduce gastrointestinal absorption of different drugs (1, 2). The ability of AC to adsorb drugs and other toxins has made administration of this compound one of the most effective methods of treating poisoned patients. However, a literature survey shows that interest in the effect of AC on the absorption and elimination of antimicrobial agents has been limited. Some workers have shown that orally administered AC can inhibit the gastrointestinal absorption of tetracycline, doxycycline, trimethoprim (3-5), and chloroquine (6).

To investigate the effect of ingested charcoal on the pharmacokinetics of antimicrobials, we monitored the effect of AC on the gastrointestinal absorption and excretion of rifampicin, a popular antitubercular and antileprous agent.

METHODS

Study Design

Six healthy male volunteers, aged 19 to 28, participated in the study after giving informed consent. Subjects' weights ranged from 58 to 75kg. Health status was reviewed with a medical history. Subjects were not taking any prescribed medications, had no sensitivity to rifampicin or AC, had no history of leprosy or tuberculosis, and had not consumed rifampicin within one week of the study.

The study was initiated with a single oral dose of 600mg of rifampicin (Ciba Geigy), equivalent to four standard-dose rifampicin capsules, along with 350ml of water. The study commenced at 0800 hours after an overnight fast.

One and two weeks later, the subjects ingested the same dose of rifampicin, immediately followed by 7.5 and 15g of AC (Ultrasorb Merck) slurry in 350ml of water, respectively. Between each phase a one-week washout period was employed. The volunteers did not eat for six hours after rifampicin ingestion. No other attempt was made to control or restrict diet during the study period.

The protocol for the study was reviewed and approved by the Human Experimental and Toxicology Procedures Committee of our institution.

Assay:

Urine collections were made just before and at 1, 2, 4, 8, 12, 24, and 36 hours after rifampicin intake in each of the 3 tests. The
volume of the urine samples collected were recorded and 2ml aliquots were stabilized with 0.2ml of toluene, then frozen at-20°C until analysis. Urine rifampicin concentrations were determined by a spectrophotometric method. Urine samples (0.5ml) were added to test tubes containing 1ml of distilled water and 1.5ml of phosphate buffer (pH 7), after which 2.0ml of iso-amyl alcohol were added. The samples were then analyzed at 475nm, using a SP/6 Pye Unicam spectrophotometer (7).

A calibration curve was produced using rifampicin concentrations of 200, 100, 50, 25, 12.5, 6.25 and 3.125mg/ml.

Pharmacokinetic Calculations:

For each subject a plot of the cumulative amount of rifampicin excreted in urine against sampling time was produced. The amount of rifampicin recovered in each of the tests was calculated from the cumulative urinary excretion, and percentage recovery was determined. The cumulative amount of rifampicin excreted was obtained by adding the amounts of the

drug excreted up to that sampling time. The excretion rate (dDU/dt) was determined using the method of Ritschel (8).

Statistical Analysis:

The differences between sample means were analyzed using Student's t-test for paired data, with statistical significance defined as p < 0.05.

RESULTS

Figure 1. shows the effect of AC on rifampicin absorption. A cumulative plot of the amount of rifampicin excreted reached a plateau at about 36 hours after the oral administration of 600mg. A similar cumulative plot of the amount of rifampicin excreted after ingestion of 600mg of the drug with 7.5 and 15g of AC showed a much lower plateau, indicative of reduced absorption of the drug.

Table 1 indicates the amount of rifampicin recovered from the urine for each of the three tests. The test group that received 15g of AC showed the least adsorption of rifampicin, with only a 1.2 per cent recovery of the drug in the

![Figure 1](image)

**Fig. 1** Amount of rifampicin recovered (mg) in urine at each collection interval (600mg rifampicin per os at t=0).
Table 1 Amount of Rifampicin Recovered from Urine (N-6)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Rifampicin Alone</th>
<th>Rifampicin and 7.5g AC</th>
<th>Rifampicin and 15g AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered (mg)</td>
<td>78.70 ± 2.34</td>
<td>24.96 ± 2.02</td>
<td>7.40 ± 1.3</td>
</tr>
<tr>
<td>Percent Recovery</td>
<td>13.1</td>
<td>4.2</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SEM
Significance was established using Student's t-test.

Fig. 2 Effect of activated charcoal on the excretion rate of rifampicin.

Effect of Activated Charcoal on Rifampicin Absorption in Man

DISCUSSION

To our knowledge, this is the first quantitative study of the effect of AC on rifampicin absorption and excretion in man. It was designed to investigate the effect of AC (7.5 and 15g) on the excretion of a therapeutic concentration of rifampicin. It is evident from this study that AC can adsorb rifampicin in vivo.

Levy and Tsuchiya 1972 showed that there was a dose-dependent increase in the efficacy of AC. The 13 percent recovery in control subjects and 4.2 and 1.2 percent recoveries of rifampicin after administration of 7.5 and 15g of AC, respectively, clearly confirm Levy and Tsuchiya's findings. The percentage control urinary excretion (13%) of orally administered rifampicin obtained in this study is lower than the reported normal percentage urinary excre-
This may be due to more extensive metabolism as a result of slower presentation of the drug to the liver during the first passage. The decreased excretion rate with increasing amounts of AC observed in this study is also in conformity with previous observations on chloroquine and charcoal (6).

It might be argued that the immediate administration of activated charcoal in our study does not represent a typical clinical condition since there is usually a time lag before management is instituted in cases of poisoning. Nevertheless the observation that both the amount of rifampicin recovered and excretion rates showed significant reductions raises the possibility that the AC can still "catch up" even if administered some hours after rifampicin administration (9).

REFERENCES