Chlorpromazine Metabolism. IX.
Pharmacokinetics of Chlorpromazine Following Oral Administration in Man

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A single oral dose (120 mg/m²) of chlorpromazine hydrochloride was administered to four healthy subjects and the blood levels of chlorpromazine were determined with time. Appropriate equations describing the two-compartment open model with zero-order absorption and the two-compartment model with first-order absorption, both with a lag time, were fitted to the observed data using weighted nonlinear least-squares regression analysis. Fitting the two-compartment model with zero-order absorption and a lag time to the observed data resulted in a significant reduction of the weighted sum of squared deviations, i.e., better correlation between the observed and calculated data, and a closer random scatter of the observed concentration data around the calculated curve with no apparent systematic deviations from the curve. These results suggest that chlorpromazine absorption is zero order. Chlorpromazine began to appear in the systemic circulation after a mean lag time of 0.4 hr and continued to be absorbed for approximately 2.9 hr. The mean half-lives of the distribution and elimination phases were 1.63 and 17.7 hr, respectively.

KEY WORDS: chlorpromazine; pharmacokinetics; oral absorption; single dose.

INTRODUCTION

Although chlorpromazine (CPZ) metabolism in man has been studied extensively (1-11), its pharmacokinetics has not been well defined. No information has been reported pertaining to the kinetics of CPZ absorption

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in man, and relatively little has been reported concerning its kinetics of
distribution and elimination. The absorption of orally administered CPZ
has been reported to be incomplete, with 10–80% of the dose reaching the
systemic circulation intact (4,5). The peak CPZ concentration usually
occurs 2–4 hr after administration (4,6,8,10), and its terminal elimination
half-life has been reported to range from 3 to 60 hr (2,4,6–10).

This report presents data on the apparent absorption and elimination
kinetics of orally administered CPZ and its urinary excretion in healthy
volunteers.

MATERIALS AND METHODS

Chemicals and Assay Procedures

The chemicals, assay methodology, and application of the
methodology used in the analyses of the blood and urine samples have
been described previously (12–16). However, a modification of the extrac-
tion step of the procedure was necessary to accommodate the use of a 9-ml
sample for assay. This consisted of using 6 ml of 2 N sodium hydroxide to
adjust the blood to >pH 13 and then extracting with 20 ml of n-hexane
containing 1.5% isoamyl alcohol.

Criteria for Subject Selection

The subjects in this study were four male inmates of the Oklahoma
State Penitentiary at McAlester, Oklahoma. They were selected for study
after passing a physical examination demonstrating no evidence of active
disease and after passing a laboratory survey consisting of a hemoglobin,
 hematocrit, red and white blood count, differential, platelet estimate,
urinalysis, serum total and direct bilirubin, SGOT, SGPT, alkaline phos-
phatase, creatinine phosphokinase, total serum protein, serum albumin,
fasting blood sugar, BUN, creatinine, and uric acid. All the above tests
were repeated on day 3 of the study. Subjects had no significant past
history of gastrointestinal, liver, renal, or cardiovascular disease, and had
received no medication of any kind during the previous 2 weeks. All
subjects were informed of the nature of the study, of all foreseeable and
known hazards, and of their right to withdraw at any time; only then were
they asked for written consent.

Pharmacokinetic Procedures

All subjects were housed on the study ward of the McAlester Division
of Clinical Pharmacology, The University of Oklahoma Health Sciences