Keyphrases □ Propranolol—nasal absorption in humans □ Absorption, nasal—propranolol, humans

To the Editor:

Propranolol, an adrenergic β-receptor-blocking drug, is widely used for hypertension management and treatment of angina pectoris. However, the drug is absorbed inefficiently and variably from oral dosage forms. A study in humans showed that the oral administration of propranolol results in considerable variation in plasma drug levels. Peak plasma levels in five subjects given 80-mg oral doses varied sevenfold, while those in the same subjects given 10-mg iv doses varied only twofold (1). Furthermore, drug bioavailability of an 80-mg oral dose in some subjects, as calculated from the ratio of the area under the curve, was as low as 16% of the bioavailability of a 10-mg iv dose. The variations in the blood levels as well as the low bioavailability for oral doses have been attributed to extensive drug metabolism in the GI tract during absorption and to the first-pass effect (2, 3).

Previous studies in rats (4) and dogs (5) showed that propranolol is absorbed rapidly and completely from the nasal mucosa. We now report the results of a study of the nasal absorption of propranolol in humans.

Six healthy male subjects, 21–35 years old, were selected for participation in a randomized crossover study after providing written informed consent. The subjects were admitted to the clinical facility following an 8-hr fast, and dosing commenced in the morning (7:00 am).

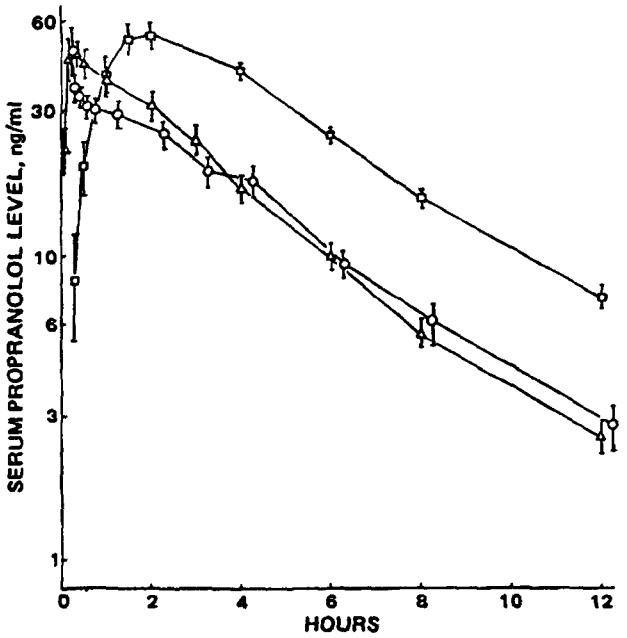

Figure 1—*Time course of the average serum propranolol levels in six male subjects following nasal administration of 10 mg/subject (△), intravenous administration of 10 mg/subject (○), and oral administration of 80 mg/subject (□).*

Table I—Mean Area under Serum Level–Time Curve for Propranolol Administered by Three Routes

Route	Mean $AUC_{0-\infty} \pm SE$, (ng × hr)/ml	$\frac{AUC_{oral,nasal}\ dose_{iv}}{AUC_{iv}\ dose_{oral,nasal}}$
Intravenous (10 mg)	175.4 ± 20.4	—
Nasal (10 mg)	190.3 ± 17.6	1.09
Oral (80 mg)	349.5 ± 35.2	0.25

For the oral administration, two 40-mg propranolol hydrochloride tablets[1] were dissolved in 30 ml of water, followed by 150 ml of water. For the intravenous administration, 10 ml of propranolol hydrochloride injection[2] (each milliliter contained 1 mg of propranolol hydrochloride) was infused at a rate of 0.73 mg/min. For the nasal administration, 10 mg of propranolol hydrochloride in 0.2 ml of 2% methylcellulose[3] gel was placed in the nasal cavity using a 1-ml syringe while the subjects were in a sitting position.

Blood samples were obtained periodically after drug administration, and the serum was separated immediately and frozen until analysis. The serum drug levels were determined spectrophotofluorometrically (3, 4).

Figure 1 shows the mean serum propranolol levels for the three administration routes. Table I lists the area under the serum level–time curve (AUC) and the adjusted AUC ratio.

As shown in Fig. 1, the serum drug levels after intravenous and nasal administration of 10-mg doses were identical. The oral bioavailability calculated from the adjusted AUC ratio was 25%.

The results also indicate that propranolol hydrochloride is absorbed rapidly from the nasal mucosa. The nasal route for propranolol administration appears to be superior to the oral route and as effective as the intravenous route.

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[1] *Inderal tablets, lot 1JRB, Ayerst Laboratories.*
[2] Inderal injection, 1 mg/cm³, lot 1LAF, Ayerst Laboratories.
[3] Methocel, Dow Chemical Co.

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