

10708 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

tissue binding. In subjects with normal renal function digoxin is excreted exponentially with an average half-life of 36 hours resulting in the loss of 35-40 percent of the body stores daily.

Serum levels and pharmacokinetics are essentially unchanged by massive weight loss suggesting that lean body mass should be used in dosage calculations. The peak blood level from oral dosing with tablets occurs 1-3 hours after administration. The onset of therapeutic action of digoxin after oral tablets is 1-2 hours with the peak therapeutic effect occurring 6-8 hours after dosing.

INDICATIONS

1. "Congestive heart failure," all degrees, is the primary indication. The increased cardiac output results in diuresis and general amelioration of the disturbances characteristic of right (venous congestion, edema) and left (dyspnea, orthopnea, cardiac asthma) heart failure.

Digitalis, generally, is most effective in "low output" failure and less effective in "high output" (bronchopulmonary insufficiency, infection, hyperthyroidism) heart failure.

Digitalis should be continued after failure is abolished unless some known precipitating factor is corrected.

2. "Atrial fibrillation"—especially when the ventricular rate is elevated. Digitalis rapidly reduces ventricular rates and eliminates the pulse deficit. Palpitation, precordial distress or weakness are relieved and any concomitant congestive failure ameliorated.

Digitalis is continued in doses necessary to maintain the desired ventricular rate and other clinical effects.

3. "Atrial flutter" digitalis slows the heart and regular sinus rhythm may appear. Frequently the flutter is converted to atrial fibrillation with a slow ventricular rate. Stopping digitalis at this point may be followed by restoration of sinus rhythm, especially if the flutter was of the paroxysmal type. It is preferable, however, to continue digitalis if failure ensues or if atrial flutter is a frequent occurrence.

4. "Paroxysmal atrial tachycardia" digitalis may be used, especially if it is resistant to lesser measures. Depending on the urgency, a more rapid acting parenteral preparation may be preferable to initiate digitalization, although if failure has ensued or paroxysms recur frequently, digitalis is maintained by oral administration.