Intramuscular Administration of Digoxin in Propylene Glycol.* (23217)

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Injection of common digitalis glycosides by the intramuscular route has been restricted by two limiting factors: Many of the glycosides dissolve poorly in water, while solvents that are effective also irritate the site of injection. Experience with propylene glycol as a vehicle for intramuscular injection(1,2) led to its trial with the digitalis glycosides. The preparation described in this report contained digoxin, 0.25 mg per cc, in 40% propylene glycol and 10% ethyl alcohol.¶ Onset and persistence of cardiac action were compared after injection by the intravenous and by the intramuscular route. Local reactions were examined after injections of intramuscular digoxin, and after injections of the solvent.

Method. Cardiac effect was measured in patients with auricular fibrillation, as described in detail elsewhere(3). Seven patients who maintained rapid ventricular rates without digitalis were placed at complete bed rest in the hospital. The etiology of their heart disease varied, their ages ranged from 34 to 75 years, and 4 were female. None had gross edema. After one or 2 weeks, when the apex rate had declined to a constant level, an injection of digoxin was given and the rate followed closely. In another week or 10 days the second injection of digoxin was given by the alternate route. In every case the dose was 1.2 mg, the full digitalizing dose of digoxin(3). Each patient received an intramuscular and an intravenous dose, the order being reversed in 3 of the 7 subjects. Additional injections were made for systematic study of the local reactions by a method previously described(4). Each of 26 ambulant patients not on digitalis received an injection deep into the buttock muscle, and a week later a second injection into the opposite buttock. One injection was 2 cc of the digoxin solution, the other 2 cc propylene glycol, and the sequence random. The physician who questioned them and examined the site did not know which material had been injected.

Results. The curves in Fig. 1 demonstrate the more gradual onset of digoxin effects following intramuscular injection. At 1 hour, when the activity of intravenous digoxin was virtually complete, that of intramuscular digoxin was just perceptible. Maximum effect reached the same intensity for the 2 routes, though present by 2 hours after intravenous injection and not until 8 hours after intramuscular injection. The apex beat returned toward control level at the same rate whether the injection was intramuscular or intravenous.

Variability in the effect was studied from

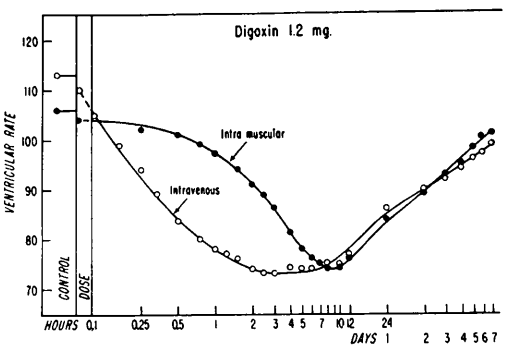

FIG. 1. Development and persistence of cardiac action in 7 patients with auricular fibrillation. Horizontal bars in space labeled "control", are average rates after one to 2 weeks of bed rest. "Dose" represents 6 minutes for intravenous injection, after which the logarithmic scale begins.

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¶ "Lanoxin" brand digoxin, supplied by Burroughs Wellcome & Co.

TABLE I. Local Reactions to Intramuscular Injection.

% of 26 patients with	Time of examination: 1 hr	Days: 1	2	3	7
	Digoxin preparation				
Severe pain	50	15	0	0	0
Erythema	0	8	12	8	0
Induration	0	42	4	4	0
	Propylene glycol				
Severe pain	4	0	0	0	0
Erythema	0	0	0	0	0
Induration	0	23	8	4	4

each of the 14 individual ventricular rate curves. The deepest depression of rate sustained for at least 3 hours was read from each curve. That depression fell lower after intravenous injection in 4 patients, after intramuscular in 3. The mean effects for the routes were not different; standard errors were 2.5 beats per minute for intravenous and 3.6 for intramuscular. No systemic toxicity was encountered.

Table I summarizes the local reactions and their time of onset. Within 1 hour of intramuscular digoxin half of the patients developed severe pain, and most of these showed tissue reactions the following day. In the parallel test, propylene glycol caused little pain and less frequent tissue response. Twenty additional patients served in a final "double-blind" comparison between reactions to the solvent (40% propylene glycol and 10% ethanol) and to physiological saline. In these 20 patients there was neither tissue reaction nor severe pain, although 9 of them mentioned fleeting pain after the solvent and 3 did so after saline.

Discussion. Absorption from an intramuscular depot of digoxin is not fast enough to serve an emergency that demands rapid digitalization. This preparation might act as a convenient substitute for oral digoxin in patients temporarily unable to take regular digoxin tablets. Since only two-thirds of the activity of oral digoxin is detected on the heart(3), a shift from oral to intramuscular digoxin should include reduction in dosage.

Summary. Digoxin in 40% propylene glycol and 10% ethanol was injected intramuscularly in 7 patients with auricular fibrillation. Its full cardiac effect was reached in 8 hours, while intravenous digoxin in the same patients reached full effect in 2 hours. Intensity and persistence of action were the same for both routes. Additional intramuscular injections in 26 patients revealed pain but no permanent tissue damage.

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Intestinal Absorption of Pyrimidines in the Rat.* (23218)

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Continuing interest in the metabolism and pharmacology of pyrimidines and pyrimidine derivatives(1,2) prompted us to make a study of the intestinal absorption of a number of 2-thiopyrimidines and of 3 natural pyrimidines. Compounds of this type have frequently been studied by oral administration to animals, although it has not been determined which of them is adequately absorbed from the gastrointestinal tract. We wished

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