we suggest that patients on this drug should be carefully assessed regularly so that lesser degrees of muscle weakness are not overlooked.

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[1] *Drug and Therapeutic Bulletin*, 1976, **14**, 97.
[2] Lockhart, J D F, and Masheter, H C, *British Journal of Clinical Practice*, 1976, **30**, 172.
[3] Howard, D J, and Russell Rees, J, *British Medical Journal*, 1976, **1**, 133.
[4] L'Hermitte, F, *et al*, *British Medical Journal*, 1976, **1**, 1256.

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Severe thrombophlebitis with Praxilene

Intravenous or intra-arterial naftidrofuryl oxalate (Praxilene) infusions are used in patients with vascular insufficiency for rest pain and pregangrene or trophic ulceration. For intravenous use it is recommended that 200 mg (25 ml) of naftidrofuryl should be infused over one and a half to two hours diluted with 200 ml of dextrose, dextrose-saline, or low-molecular-weight dextran. In our early experience with this regimen we found that patients rapidly developed severe thrombophlebitis in the infused veins. This led us to perform a prospective survey of patients who had naftidrofuryl infusions. In most cases the thrombophlebitis necessitated one or more changes of drip site so that 13 infusions in seven patients were ultimately available for analysis.

Patients, methods, and results

Seven consecutive patients who were given naftidrofuryl infusions were studied. In each case the indication was severe lower limb ischaemia with rest pain in an elderly patient (five men and two women). A standard dose of the drug was given twice daily (200 mg in about 200 ml of dextrose or saline). The infusion site was inspected after each dose by one of us: the area of any erythema or thrombosis was measured and the patient asked about pain. The investigator did not influence the treatment or selection of drip sites, and in some cases the infusion was continued after the first signs of inflammation had appeared (see table).

Ten cases of thrombophlebitis occurred in 13 infusions (see table). The affliction was far more severe and developed far more rapidly than infusion thrombophlebitis seen with dextrose 5% or saline alone. All but one patient (case 7) had at least one episode. The two women were less severely affected, though the numbers were too small to show a significant difference. In six cases the first sign occurred after only one dose of the drug—that is, after about two hours of infusion. Fortunately the condition resolved after the cannula was removed. The pain was severe in some cases and was relieved with kaolin poultice and mild oral analgesics. The inflammation settled over about 48 hours but all patients were left with the "cord" of thrombosed vein. No cases of suppurative thrombophlebitis occurred.

Comment

Mild thrombophlebitis is a common complication of intravenous infusions: the reported incidence is between 12% and 39%, but it may approach 100% if the infusions are continued for long enough. In the cases reported here the thrombophlebitis began after only short periods of infusion and was particularly severe. We believe that this is an effect of naftidrofuryl.

The aetiology of thrombophlebitis is multifactorial. The low pH of naftidrofuryl (2·75) and the diluting fluid may be relevant. Commercial dextrose 5%, for example, has a pH around 4·2, but if the pH is raised to a physiological level the incidence of thrombophlebitis is dramatically reduced.[1] Naftidrofuryl 200 mg in 200 ml of dextrose-saline has a pH of 3·4.

With naftidrofuryl, however, the inflammation began very early (often during the first two hours), and this is not a characteristic of infusions with dextrose or saline alone. It has long been recognised that the thrombophlebitis rate increases with the duration of the infusion, but Elfring, in a large series, recorded a very low complication rate in infusions lasting less than two hours, and the few cases of thrombophlebitis were mild.[2]

Some patient factors predispose to infusion thrombophlebitis, but these were not found consistently in our cases: they include severe illness,[3] middle age,[1 2] the female sex,[2] adjacent infection,[3] and burns.[4] Our patients were in an advanced stage of peripheral vascular disease but were otherwise well. Their advanced age might have been protective.[1] Immune deficiency states have been associated with this condition,[4] but, although the immune status of our patients was not investigated, we have no reason to suppose that any abnormality existed.

The frequency and severity of the reactions that we observed were probably due to some factor in naftidrofuryl other than the pH. Several studies have shown the damaging effects of drugs added to infusions and different factors are entailed with each drug.[5] To clarify the effects of naftidrofuryl we are undertaking animal studies. In the meantime it would seem wise when infusing naftidrofuryl to change the drip site often, if possible after each dose. It is not yet clear whether naftidrofuryl has any effect on the central veins, and infusion into these should be undertaken with caution.

[1] Fonkalsrud, E W, *et al*, *Surgery*, 1968, **63**, 280.
[2] Elfring, G, Hastabacka, J, and Tammisto, T, *American Heart Journal*, 1967, **73**, 717.
[3] Todd, R M, *Lancet*, 1951, **1**, 982.
[4] Stein, J M, *New England Journal of Medicine*, 1970, **282**, 1452.
[5] Turco, S J, *Bulletin of the Parenteral Drug Association*, 1975, **29**, 89.

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Local thrombophlebitis after administering naftidrofuryl 200 mg by infusion over one and a half to two hours

Case No	Sex	Cannula (gauge and type)	Diluent	Drip site*	Pain	Area of erythema (mm)	Length of thrombosis (mm)	No of doses given	No of doses before first sign	Severity†
1	M	18, Medicut	5% Dextrose	R forearm	+ +	300 × 40	300	3	1	S+
				L forearm	+ + +	175 × 60	175	3	1	S+
2	M	Butterfly	Dextrose	L hand	−			1		O
		18, Medicut	Saline	L forearm	+ + +	170 × 50	170	2	1	S+
				R forearm	+ +	140 × 50	140	2	1	S
3	M	18, Medicut	5% Dextrose	R forearm	+	Minimal	115	8	8	S
4	F	18, Medicut	Isotonic saline	L forearm	+	130 × 30	130	6	2	S
			Dextrose-saline	R forearm	−			1		O
5	M	18, Medicut	Isotonic saline	L forearm	+	85 × 40	140	5	2	S
				R forearm	+	210 × 50	100	4	1	S
6	M	18, Medicut	5% Dextrose	LACF	+ +		220	2	2	S+
				RACF	+ +	210 × 50	210	4	1	S+
7	F	18, Medicut	Dextrose-saline	L hand	−	Minimal		2	2	O

*L(R)ACF = Left (right) antecubital fossa.
†S+ = Very severe. S = Severe. O = None.