she admitted that she swallowed large quantities of the laxative Dorbanex in the belief that she had severe constipation. Witnesses had noted yellow streaks around the mouth, which came from this drug. She was advised to stop taking Dorbanex and to rely on another laxative. This she agreed to do after many exhortations. Eventually, after some months, the blue colour of the skin faded and its normal colour was restored.

Discussion

After the initial negative findings, our investigations centred on the laxative Dorbanex. Its two constituents are (a) poloxamer 188, which is virtually unabsorbed from the gut and thus excreted in the faeces, and (b) danthron, which is a synthetic anthroquinone compound, allied chemically to cascara, senna, rhubarb, and aloes, with an action on the nerve endings of the myenteric plexus to stimulate the muscle of the intestine. Side effects are recognised as a temporary but harmless pink or red colouring of the urine with discoloration of the perianal skin and occasionally of the mucosa of the large intestine.

The interest in this case stems from the greyish-blue colour of the skin in contrast to the pink colour of the plasma. Possibly some interaction between the danthron component of the laxative and phenolphthalein, which she also took in excess, might account for the blue colour, although no colour change occurred on mixing the two in the laboratory. Subsequently, phenolphthalein was added to the urine of another patient taking Dorbanex. No colour change occurred at pH 7.4 or at 8.5. At pH 9.0 an orange colour appeared and above pH 9.4 this became an increasingly deeper red. It could not be established that there was a relation between Dorbanex and other drugs which were present in the blood as a result of treatment of the mental instability. Animal studies were deemed of no value. None the less, despite the obsessional use of a laxative, the rarity of the condition does suggest that a special relationship may have existed.

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Symptomatic and objective effects of venesection on patients with intermittent claudication

There is no standard medical treatment for intermittent claudication. Reconstructive surgery is suitable only in a small proportion of patients and the results are not satisfactory. Blood flow may be increased by reducing whole blood viscosity.^{1 2} Beneficial effects have

been described in patients with ischaemic heart³ and brain disease after venesection, in both polycythaemic⁴ and in haematologically normal patients.⁵ Theoretical and epidemiological grounds suggest that blood flow and oxygen supply continue to improve as the haematocrit value falls well beneath normal limits. We wished to discover whether measurable benefit was observed after venesection among patients with severe calf claudication.

Patients, methods, and results

Nine patients who developed calf pain within a 200-yard (180 m) walk at their customary speed were selected (see table for details). They had no other clinical features of ischaemic disease. 500 ml of blood was withdrawn from these patients at fortnightly intervals on three occasions. Assessment was made before the first venesection and a fortnight after the final venesection. They indicated whether they experienced any change and were objectively assessed on the following criteria:

Claudication count—The subject "walked" up and down three 9-inch (22.5 cm) steps at a rate of one step per second. The "claudication count" was the time in seconds before the onset of calf pain.

Venous occlusion plethysmography—Arterial blood flow to the calf was measured both before and after two min of arterial occlusion, using mercury-in-rubber strain gauge plethysmography.

Ankle to arm systolic pressure index—This pressure ratio was measured before and immediately after a standard exercise (one step per second, as described above, for one minute). The time required for ankle pressures to return to a new resting value was also recorded.

The results are shown in the table.

Discussion

These preliminary data fail to indicate that it would be fruitful to extend the study. Moreover, there is no indication that venesection to a predetermined haemoglobin concentration would be a more promising approach. If we relate a benefit score derived from the observed changes to the haemoglobin concentration reached after venesection we fail to show any relation between benefit and haemoglobin concentration. There is convincing evidence that reducing raised haemoglobin concentrations in subjects without peripheral vascular disease improves blood flow. Nevertheless, the occlusive lesions in our patients are such that blood flow occurs through the collateral vessels. Under these circumstances a fall in haemoglobin concentration appears to have no consistent effect.

¹ Dormandy, J A, *British Medical Journal*, 1971, **4**, 716.

² Messmer, K, *et al*, *European Surgical Research*, 1972, **4**, 55.

³ Burch, D E, and DePasquale, H P, *Diseases of the Chest*, 1965, **48**, 225.

⁴ Thomas, D J, *et al*, *Lancet*, 1977, **2**, 161.

⁵ Thomas, D J, *et al*, *Lancet*, 1977, **2**, 941.

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Case No	Age and sex	Hb		PCV		CT		Subjective change		MRF		PF		Systolic blood pressure ankle/brachial (mm Hg)		Recovery time (min and s)	
		Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	62 M	15.0	12.2	47	37	1.15	1.20	0	0	8.5	10			115/170	90/150	2	5
2	62 M	13.6	12.5	42	38	>4	>4	0	0	6	7			100/140	90/125	3	10
3	69 M	16.5	14.4	49	41	2.30	>5	0	+	6	5.5	9.3	4.3	110/130	110/	4	1
4	66 M	14.1	10.7	44	34	>5	>5	0	+	3.5	5.7	4.5	16.0	150/180	100/145	20	4.20
5	67 M	16.0	11.6	49	35	3.30	1.0	0	+	7.3	11.0	16.5	12.0	90/	75/145	6	6.30
6	59 F	14.9	12.7	45	39			0	0	6.3	8.5	10.4	17.8	80/	80/110	3.30	4
7	55 F	13.3		40		1.30	1.15	0	0	6.8	4.0	3.8	5.2	90/100	80/130	1	1.30
8	65 M	16.7	14.8	50.5	45	1.20	1.45	0	0	1.9	3.7	5.3	5.3	70/160	85/140	5.30	3
9	66 M	12.9	12.4	40	38	1.30	0.50	0	0	3.2	2.3	9.0	7.5	120/210	125/210	4	

CT = Claudication time. MRF = Mean resting blood flow. PF = Peak blood flow.