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Effect of prolonged infusion on vein calibre: a prospective study

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Infusion thrombophlebitis is common and is the principal limitation to intravenous nutrition (IVN) via a peripheral vein, yet its precise pathogenesis is unclear. Prospective observations were performed on patients in whom a hypertonic, acidic, nutritional emulsion was infused via fine-bore polyurethane catheters placed in peripheral veins. B mode ultrasound was used to determine vein calibre and proved to be a useful means for serial examination during intravenous infusion. Contrary to previous reports, no evidence of venospasm was observed. It is suggested that previous evidence of venoconstriction is erroneous and that other mechanisms are responsible for thrombophlebitis.

It has been proposed that infusion thrombophlebitis is the consequence of venospasm *(1)*. Others have postulated that glyceryl trinitrate (GTN) ointment deters infusion thrombophlebitis *(2–4)* through venodilatation. However, vein diameter has never been measured during peripheral intravenous infusion. A prospective study was performed whereby peripheral veins, through which intravenous nutrition (IVN) was continuously infused, underwent serial ultrasonic measurement of their diameter.

Method

All patients received a standard complete nutritional emulsion (1800 kcal, 13 gN, 2500 ml, 1100 mmol/kg, pH 6.4) *(5)*. Constant feed infusion, at a flow of 108 ml/h, was maintained with a volumetric pump (Ivac 560®, Ivac Corporation, San Diego, California, USA). It was delivered via fine-bore polyurethane catheters (Hydrocath®, Ohmeda, Swindon, UK) inserted 15 cm into arm veins at the antecubital fossa. The arm with the most prominent virgin vein was selected and catheters inserted by the Seldinger technique *(6)*. Catheters were inspected twice daily and removed at the first symptom or sign of thrombophlebitis *(7)*, or on elective cessation of IVN. The feed contained heparin (Heparin Injection BP 1500 iu, Leo Laboratories Ltd, Princes Risborough, UK) and hydrocortisone (Efcortisol® 15 mg, Glaxo Laboratories Ltd, Greenford, UK). A 5 mg GTN patch (Transiderm Nitro®, Ciba Laboratories, Horsham, UK) was placed over the position of the catheter tip and changed daily.

A Diasonics Spectra® ultrasound scanner (7.5 MHz transducer, supplied by Sonotron Ltd, Bedford, UK) was used. Acoustic coupling was maintained with Aquasonic 100® gel (Parker Laboratories, Orange, New Jersey, USA). Observations were performed in a vascular laboratory at constant temperature (median 24°C, interquartile range 23–25°C). When clinical conditions allowed, ultrasound examination was performed before catheterisation and then immediately afterwards (day 1). Before catheterisation, the maximum anteroposterior diameter of the vein to be used was measured at two points: where the catheter would enter the vein and 15 cm proximally, where the tip would lie. There were no failed catheterisations. After catheterisation, vein diameters were measured at the point of venepuncture and the position of the catheter tip. Intravenous thrombus was recognised by previously defined criteria *(8)*. If complications did not occur, imaging was performed on days 7, 10, 15 and 20. When thrombophlebitis intervened, or the patient no longer required IVN, re-examination was performed before catheter removal. All measurements were made by a single trained vascular technician and feed infusion was not interrupted during examination. Data were analysed using SPSS for Windows® 6.0 (SPSS Inc, Chicago, Illinois, USA). Differences in vein diameters were compared by two-tailed Student's paired *t* test *(9)*. Data are quoted as mean diameters, with the 95% confidence interval (CI) for the mean difference.

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Results

In all, 22 catheters were inserted in 20 patients (14 male, 6 female, median age 62 years (interquartile range 50–76 years) (Table I). Two patients were catheterised twice, each in contralateral arms. Thirteen basilic and nine cephalic veins were used. Thrombophlebitis developed in nine catheters (mean time to onset 6 days, interquartile range 4–8.5 days), the remainder were removed without complication on cessation of IVN (median duration 11 days, interquartile range 7–16 days). Thrombophlebitis occurred more frequently in the cephalic vein (six of nine) than in the basilic vein (three of 13). In 13 arms, diameters were measured before and immediately after catheterisation. In nine cases, patients could not attend the vascular laboratory before catheterisation because of conflicting clinical imperatives.

The measurements made before and immediately after catheter insertion are summarised in Table II. Before catheterisation, the mean diameter of basilic veins was maintained along their length, whereas cephalic veins tended to narrow proximally. Mean vein diameter was slightly greater after catheterisation at the point of venepuncture, but the difference was not statistically significant. At the position of the catheter tip, mean vein diameter was larger after catheterisation and the difference was statistically significant. The effects of prolonged infusion are described in Table III. IVN infusion lasted for at least 7 days in 11 cases. Mean vein diameter was greater on day 7 at both the point of venepuncture and at the catheter tip, but the differences were small and not statistically significant. When catheters removed because of complication were considered, mean vein diameter was significantly greater on the final day of

Table I. Choice of vein, duration of infusion, and clinical outcome

Patient	*Vein*	*Duration (days)*	*Precatheterisation scan*	*Outcome*
P1	Basilic	11	Yes	Uncomplicated
P2a	Basilic	6	Yes	Thrombophlebitis
P2b	Basilic	7	Yes	Uncomplicated
P3	Basilic	10	Yes	Uncomplicated
P4	Cephalic	7	Yes	Uncomplicated
P5	Cephalic	5	Yes	Thrombophlebitis
P6	Basilic	20	Yes	Uncomplicated
P7a	Basilic	15	Yes	Uncomplicated
P7b	Cephalic	10	No	Thrombophlebitis
P8	Cephalic	4	Yes	Thrombophlebitis
P9	Basilic	20	Yes	Uncomplicated
P10	Basilic	17	Yes	Uncomplicated
P11	Cephalic	4	Yes	Thrombophlebitis
P12	Cephalic	15	Yes	Uncomplicated
P13	Basilic	4	No	Thrombophlebitis
P14	Basilic	7	No	Uncomplicated
P15	Basilic	11	No	Thrombophlebitis
P16	Cephalic	7	No	Uncomplicated
P17	Cephalic	7	No	Thrombophlebitis
P18	Cephalic	6	No	Thrombophlebitis
P19	Basilic	7	No	Uncomplicated
P20	Basilic	14	No	Uncomplicated

Table II. Comparisons of vein diameters (mm) before and immediately after catheterisation

Comparison of vein diameters measured before catheterisation

	Site of venepuncture	*Position of catheter tip*	*95% CI*	*P*
Basilic vein ($n=8$)	4.7	4.7	1.1– −1.0	0.913
Cephalic veins ($n=5$)	5.1	3.8	0.7– −3.2	0.139

Effect of catheter insertion on vein diameter

		Before catheterisation	*After catheterisation*	*95% CI*	*P*
Site of venepuncture	($n=13$)	4.9	5.1	0.7– −0.2	0.223
Position of catheter tip		4.4	5.1	1.3– −0.1	0.027

Table III. Effect of prolonged infusion on vein diameters (mm)

Comparison of vein diameters after 7 days of uncomplicated infusion					
		Day 1	*Day 7*	*95% CI*	*P*
Site of venepuncture	($n=11$)	5.2	5.6	1.0– −0.2	0.159
Position of catheter tip		5.3	5.4	0.7– −0.2	0.628
Comparison of vein diameters for catheters removed because of complication					
		Day 1	*Final day*	*95% CI*	*P*
Site of venepuncture	($n=8$)	4.9	5.8	1.8– −0.1	0.033
Position of catheter tip		4.2	5.3	2.1– −0.6	0.04
Comparison of vein diameters for catheters removed without complication					
		Day 1	*Final day*	*95% CI*	*P*
Site of venepuncture	($n=12$)	5.1	5.0	0.3– −0.5	0.513
Position of catheter tip		5.2	5.3	0.7– −0.5	0.672

infusion than on the first, at the point of venepuncture and the catheter tip. Ultrasonic evidence of intraluminal thrombus was found in every case. When uncomplicated catheters were considered, there was no significant difference in mean vein diameter between the first and final days of infusion either at the point of venepuncture or the catheter tip.

Discussion

Effect of cannulation and infusion on vein calibre

Thrombophlebitis could be triggered by trauma at venepuncture or by delivery of IVN at the catheter tip. Hence, observations were made at two points in the arm; it was envisaged that the distance between them might distinguish between events at either. The feed emulsion was hypertonic and acidic; both of these factors are recognised promoters of infusion thrombophlebitis *(10,11)*. When thrombus was detected, vein diameter tended to have increased at the point at which the clot was observed; the slight dilatation might have been owing to the thrombus itself. Contrary to expectation, venospasm was not observed in this study, either as a response to catheterisation or prolonged infusion of the irritant emulsion. There may be several explanations for this. Venospasm may have been transient and hence not detected. However, it seems improbable that the vein lumen narrowed substantially, thrombosis occurred and then stretched the vein to greater than its original diameter. GTN patches were used and it is possible that, although no substantial venodilatation occurred, they prevented venospasm. Nevertheless, thrombophlebitis was observed in 40% of veins during the study despite the use of GTN. GTN patches were associated with reduced incidences of thrombophlebitis when crystalloid *(3)*, or IVN *(4,12)* were infused via peripheral veins. The authors suggested that GTN caused venodilatation, but it is possible that the drug altered endothelial metabolism, perhaps modulating prostacyclin production *(13)*.

Heparin and hydrocortisone were added to the feed in an attempt to deter infusion-related complications, but thrombophlebitis was not prevented. The drugs might be expected to influence the development of intraluminal thrombus more than change in vein calibre, were the latter to occur. Just as with GTN ointment, all patients received the feed additives and so they do not represent conflicting variables within the constraints of the study.

In this study, thrombophlebitis occurred more frequently when catheters were inserted into cephalic rather than basilic veins. Cephalic veins tended to be narrower and to taper proximally. Patients were not randomised with regard to choice of vein, but similar observations have been made *(7)*. The endothelium may be more prone to damage by the infusion device when a narrow vein is used. In other studies, infusion complications occurred more often when narrower veins were used *(14,15)*, but in these reports assessment of vein diameter was subjective only.

Ultrasound for investigation of thrombophlebitis

Most attempts to image the events associated with thrombophlebitis in man have relied on radiological contrast studies performed only after the complication had occurred *(16,17)*. In one study *(16)*, narrowing of the vein lumen was observed and was attributed to venospasm; however, it may have been because of deposition of mural thrombus. The proximal vein was occluded with a tourniquet and one might expect that subsequent contrast injection would overcome any local increase in venous tone, whereas partial luminal obliteration by thrombus would persist. Other proposed evidence for venospasm was inferred from increases in pressure required to maintain infusion *(18)*. Measurement was performed via the intravenous cannula and therefore an increase in pressure could only be observed when the vein lumen was narrower than that of the infusion device. Resistance to infusion might be explained by obstructing thrombus rather than venospasm.

This is the first study in which vein diameter has been measured directly and prospectively during infusion.

Contrast venography is not suitable for serial investigation of infusion thrombophlebitis. The pressure of contrast injection might dilate the vein and this would be compounded if a tourniquet were used. Contrast media themselves may promote phlebothrombosis *(19–21)* and, if intraluminal contrast distribution is incomplete, vein diameter may be underestimated or thrombus assumed to be present *(22)*. Moreover, the patient would be exposed repeatedly to ionising radiation. Although isotopic methods have been used to investigate infusion thrombophlebitis *(23)*, they do not allow measurement of vein diameter. Ultrasound allows repeated observation without influencing the milieu of the vein lumen. Thrombus is identifiable, and change in vein calibre can be quantified. When animal veins were examined, good correlation was found between luminal diameters measured by ultrasound and callipers post-mortem *(24)*.

Conclusion

This study found no evidence of venoconstriction associated with prolonged infusion of an irritant emulsion, but thrombophlebitis occurred nevertheless. When infusion was complicated, intravenous thrombus was always detected. The author suggests that the initiating event was venous endothelial trauma caused either by venepuncture itself, abrasion at the catheter tip, or the delivery of the feed. More work is required to elucidate the pathogenesis of infusion thrombophlebitis; ultrasound would appear to be well suited to the purpose.

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