Transcranial Doppler Directed Dextran Therapy in the Prevention of Carotid Thrombosis: Three Hour Monitoring is as Effective as Six Hours

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Background: *six hours' monitoring by transcranial Doppler (TCD) has been successful in directing Dextran therapy in patients at high risk of thrombotic stroke after carotid endarterectomy (CEA).*
Objectives: *is 3 h of routine monitoring as effective as 6 h in the prevention of early postoperative thrombotic stroke?*
Design: *prospective, consecutive study in all patients with an accessible cranial window.*
Methods: *one hundred and sixty-six patients undergoing CEA underwent 3 h of postoperative monitoring by TCD. Any patient with >25 emboli detected in any 10 min period or those with emboli that distorted the arterial waveform were commenced on an incremental infusion of dextran 40.*
Results: *the majority of patients destined to embolise will do so within the first 2 postoperative hours. Dextran therapy was instituted in nine patients (5%) and rapidly controlled this phase of embolisation although the dose had to be increased in three (33%). No patient suffered a postoperative carotid thrombosis but one suffered a minor stroke on day 5 and was found to have profuse embolisation on TCD; high dose dextran therapy was again instituted, the embolus count rate fell rapidly and he made a good recovery thereafter. Overall, the death and disabling stroke rate was 1.2% and the death/any stroke rate was 2.4%.*
Conclusion: *three hours of postoperative TCD monitoring is as effective as 6 h in the prevention of postoperative carotid thrombosis.*

Key Words: Carotid endarterectomy; Perioperative stroke; TCD; Dextran.

Introduction

Thrombosis complicates up to 3% of carotid endarterectomies (CEA) and usually manifests itself within the first 6 postoperative hours.[1–3] In previous studies, we have shown that the introduction of a quality control programme contributed towards a sustained decline in the number of patients recovering from anaesthesia with a new neurological deficit (the intraoperative stroke), but was not associated with a parallel reduction in postoperative thrombotic stroke[4,5] which, at re-exploration, consistently revealed friable platelet thrombus within an endarterectomy zone that otherwise showed no evidence of underlying technical error.[6]

Gaunt and Roberts subsequently demonstrated that postoperative carotid thrombosis was preceded by a 1–3 h phase of sustained, asymptomatic cerebral embolisation which progressed onto clinical stroke in the majority of patients.[1–3] As a consequence, we implemented a policy of routine postoperative dextran therapy which, while abolishing all postoperative thromboses, was unfortunately associated with an increased incidence of neck haematomas and one death due to multiorgan failure which the nephrologists ascribed to the dextran therapy. In the light of this, we adopted a policy of *selective* dextran therapy in potentially high risk patients guided by TCD evidence of sustained postoperative embolisation.[7] All CEAs were subsequently monitored for 6 h, Dextran was used in 5% of patients and embolisation ceased in all and no patient suffered a carotid thrombosis.[7] However, 6 h of postoperative monitoring poses considerable logistical and staffing problems and it would be preferable to reduce this to the minimum in low risk patients. Lennard's study also showed that patients destined to embolise would do so within the first 3 postoperative hours. We therefore undertook a further prospective study to see whether adoption of a 3 h monitoring policy was associated with any increase in the incidence of postoperative carotid thrombosis.

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Materials and Methods

Between 20 August 1996 and 4 December 1997, 192 patients underwent either CEA ($n=186$) or carotid bypass ($n=6$) in the Vascular Unit at Leicester Royal Infirmary for the correction of a severe internal carotid artery (ICA) stenosis. Fifty-three patients presented with a stroke (32%), 90 suffered a TIA or amaurosis fugax (54%) while 23 were asymptomatic (14%). A unilateral ICA stenosis was present in 102 (61%), bilateral ICA severe stenoses in 35 (21%) while 29 (17%) had a contralateral occlusion. A history of previous myocardial infarction was present in 35 patients (21%), 53 (32%) were on treatment for angina, 101 (61%) were on treatment for hypertension while 23 (14%) were diabetic. Permission for this study was given by the Leicestershire Ethics Committee.

Carotid endarterectomy

Endarterectomy was performed in the same manner throughout the study by a consultant vascular surgeon (PB, RN, NL) or higher surgical trainee under supervision using normocarbic, normotensive general anaesthesia and systemic (5000 iu) heparinisation. All were routinely shunted (Pruitt–Inahara), the proximal and distal intimal steps were tacked down with 7:0 prolene (Ethicon) and all arteriotomies were closed with a Dacron patch (Vascutek). A small number of patients ($n=6$) underwent a carotid bypass using reversed saphenous vein for the correction of very high disease, gross distal kinking or the presence of an excessively thinned arterial wall following endarterectomy.

Following endarterectomy and prior to final closure of the patch, the shunt was removed, the carotid vessels flushed and irrigated with heparinised saline and then reclamped. A 5 mm segment of the arteriotomy adjacent to the origin of the external carotid artery was used for angioscopic assessment[5] of the distal ICA, proximal CCA, ECA orifice and endarterectomy zone prior to restoration of flow using a 5 mm diameter flexible hysteroscope (Olympus 1070–48). The policy of the unit was to remove any fragments of thrombus and repair any intimal flap >3 mm. Where necessary, an estimate of luminal sizing of an abnormality was based on comparison with the 2 mm diameter head of the forceps that could be passed down the instrument channel of the hysteroscope. If any abnormality required correction, the endarterectomy zone was routinely re-examined to confirm that there was no residual abnormality.

Following recovery from anaesthesia, the patient was examined neurologically and transferred to the High Dependency Unit for further monitoring. Any new neurological deficit apparent upon recovery from anaesthesia was recorded and the patient assessed by a neurologist. Postoperative complications (i.e. following a normal recovery from anaesthesia and up to 30 days thereafter) were similarly documented. Our protocol required us to investigate all patients awakening from anaesthesia with a new neurological deficit by colour duplex and TCD. The decision to reoperate was thereafter left to the discretion of the surgeon. All neurological deficits occurring in the postoperative period were investigated by colour duplex, TCD, CT scan or re-exploration and all patients assessed by a consultant neurologist.

Intraoperative transcranial Doppler monitoring

Continuous TCD monitoring of blood flow velocity in the ipsilateral middle cerebral artery (MCA) was performed using a 2 MHz pulsed wave probe (via the transtemporal window), secured with an elasticated headband and connected to a Scimed PC842 transcranial system (Scimed, Bristol, U.K.). The probe was protected from dislodgement by a detachable, semicircular metal head guard. Recording started following induction of anaesthesia and continued until the surgical drapes were removed from the patient. Data were recorded onto digital audio tape for off-line analysis with particular emphasis on the number and character (air versus particulate) of emboli detected throughout the procedure.[8,9] During the operation, research staff experienced in TCD (JS, NL) were available to supervise minor revisions to the probe position and generally advise the surgeon of unexpected phenomena. In general, we aimed to keep mean MCA velocity ≥ 15 cm/s throughout the procedure, preferably ≥ 20 cm/s.

Postoperative TCD monitoring

Twenty-six of the 192 patients in the study period were not monitored in the early postoperative period because of an inaccessible window, technical problems or because a simultaneous CEA was being performed which required the presence of the monitoring staff. Accordingly, ipsilateral MCAV data were recorded for 10 min every 30 min for 3 h in 166 patients following restoration of flow. Any patient who had ≥ 25 emboli
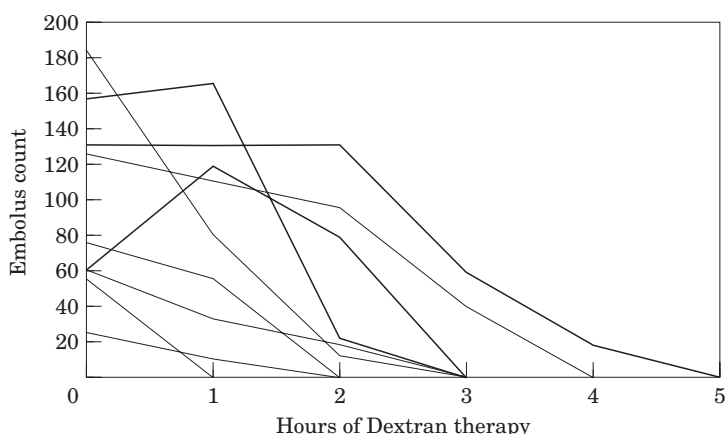
Fig. 1. Effect of dextran therapy in nine patients with either sustained embolisation or emboli which distorted the MCA waveform. The three patients who required an increase in their dose of dextran are highlighted by the bold lines. The remainder all stabilised on a base infusion rate of 20 ml/h.

detected during any 10 min period of monitoring or any patient whose emboli caused distortion of the MCA waveform (suggesting a large embolus) was commenced on an incremental intravenous infusion of dextran 40, starting at a rate of 20 ml/h. If the rate of embolisation did not diminish, the infusion was gradually increased by 5 ml/h every 10 min to a maximum of 40 ml/h. Patients receiving dextran were monitored by TCD for 6 h after restoration of flow. Once the dextran infusion rate was stabilised, it was then continued at that dose for a further 12 h.

All patients were discharged home on aspirin therapy (75 mg daily), on the fifth postoperative day, and all were reviewed 6 weeks later in the Vascular Clinic.

Results

Numbers and timing of emboli

Seventy-six patients (46%) had no emboli detected during the first 3 h of postoperative monitoring, while 79 (48%) had 1–25 emboli, seven (4%) had 26–50 emboli and four (2%) had ≥51 emboli detected. Of the 90 patients found to have one or more emboli, 43 (48%) had their first embolus detected within the first postoperative hour, 43 (48%) started to embolise in the second hour while only four (4%) had their first embolus detected in the third hour. Thus, overall 95% of those who were destined to embolise did so within the first 2 postoperative hours.

Dextran 40 therapy

Nine patients (5%) were commenced on postoperative intravenous dextran 40 therapy. Fig. 1 illustrates the effect of dextran on the ensuing embolus count. In the majority of patients the embolus count fell rapdily but in three patients, the rate of infusion had to be progressively increased either because the embolus count rate did not diminish ($n=1$) or because the embolus rate actually increased ($n=2$). However, all patients had ceased embolising whilst on the Dextran therapy. One of the nine required monitoring for 8 h overall while a further four were monitored for a total of 4 h. Thus overall, 97% of the 166 patients were monitored for only 3 h, 2% for 4 h and 1% for >4 h.

Operative morbidity and mortality

a) Intraoperative morbidity. One patient (0.6%) recovered from anaesthesia with a new neurological deficit. He had a contralateral occlusion and underwent a vein bypass for disease extending up to the skull base. During carotid clamping there was no MCA flow on TCD indicating inadequate collateralisation. Good MCA flow signals were obtained following restoration of flow but after 2 min there were increasing embolic signals and MCA velocity began to fall rapidly despite having commenced an on-table dextran infusion. Angiography revealed thrombus within the mid-portion of the graft. The shunt was reinserted, the thrombus removed and the graftotomy closed primarily after no obvious technical error was identified. Five minutes after secondary restoration of flow, profuse embolisation recurred, MCA flow again diminished towards that observed during carotid clamping and the bypass graft was again reopened after another angiogram indicated thrombus at the distal anastomosis. The graft was reopened, the thrombus removed and a vein patch inserted across the

anastomosis despite the absence of any obvious technical error. Thereafter MCA flow was maintained and no further episode of on-table thrombosis occurred. The patient subsequently recovered from anaesthesia with aphasia (but no motor deficit) which had significantly improved for him to be classed as a non-disabling stroke by day 30.

(b) Postoperative morbidity and mortality. One patient who underwent an emergency CEA for crescendo TIAs suffered a fatal myocardial infarction on day 3 despite having undergone full preoperative cardiological assessment to give an overall 30-day operative mortality rate of 0.6%. One further patient suffered a disabling stroke on day 22 following a CT scan proven intracerebral haemorrhage. Neither of these two patients had received dextran therapy in the postoperative period. One further patient received dextran in the immediate postoperative period which controlled his embolisation. However, on the fifth postoperative day he developed a monoplegia of his arm. Duplex scanning revealed a diffuse irregularity of the distal endarterectomy/ICA and TCD revealed profuse cerebral embolisation. Dextran was recommenced at 50 ml/h and this rapidly controlled the embolisation and he went on to make a full neurological recovery (grade 0 at 30 days).

Thus overall the death and disabling stroke rate was 1.2% while the death/any stroke rate was 2.4%.

Discussion

At the beginning of our research programme in 1992, we hypothesised that the implementation of a quality control programme would reduce the rate of operation related stroke through the early detection and correction of inadvertent technical error.[4] Our subsequent experience with the pilot study and a follow-up audit study in 1995 confirmed that while the quality control programme was associated with a significant fall in the rate of intraoperative stroke from 4% prior to 1992 to 0.3% by 1995,[4,5] it had little impact on the rate of postoperative thrombotic stroke which remained stubbornly at 2.7%. however, Gaunt[1,2] and Roberts[3] subsequently demonstrated that postoperative carotid thrombosis is preceded by a phase of asymptomatic but sustained micro-embolisation that could be detected by TCD. At the time we had no facility for extending the TCD monitoring into the early postoperative period and we therefore decided to administer dextran (an antiplatelet agent) to all patients postoperatively. Unfortunately, while this policy abolished carotid thrombosis it was associated with a rise in the number of

neck haematomas requiring re-exploration and one patient died of multiorgan failure which was specifically attributed by the nephrologists to our use of dextran.

Faced with this, we implemented a revised protocol in October 1995 whereupon dextran was only given to patients with sustained embolisation (≥ 25 emboli in any 10 min period during a 6 h phase of TCD monitoring) and who were therefore considered high risk for thrombosis. In this pilot study, 5% of patients required dextran therapy and embolisation ceased in all. More importantly, no patient suffered a carotid thrombosis in that series. However, implementing a routine policy of 6 h of TCD monitoring after CEA poses important logistical problems, not least manpower. We therefore undertook a second study which took advantage of an observation that was made during Lennard's original work. It was noted that >95% of patients who were destined to embolise would do so within the first 3 postoperative hours.[7] We therefore hypothesised that it may be feasible to reduce the postoperative monitoring to 3 h without significantly increasing the risk of postoperative thrombosis.

The findings of this latest study appears to support our hypothesis. The vast majority of patients (96%) who are destined to have any emboli will start within 2 h but very few (5%) will require intervention with dextran. No patient in this series suffered a stroke due to a carotid thrombosis within 30 days of surgery. These findings therefore suggest that 90–95% of low risk patients require only 2–3 h of monitoring while 5–10% higher risk patients might require longer periods of assessment. Our evidence suggests however that only 1% will require prolonged monitoring beyond 4 h.

This study has also shown that no single dose of dextran will guarantee control of postoperative embolisation. In this series, three of the nine patients (33%) required progressive increments in their Dextran therapy in order to control the embolisation and this is in accordance with our experience in the earlier pilot study.[7] This therefore suggests that implementation of a routine policy of postoperative dextran therapy will probably reduce the overall risk of postoperative carotid thrombosis but it will almost certainly not abolish it. Moreover, this study is the first to demonstrate that certain patients may start to re-embolise after some days have passed. This particular patient was high risk for re-exploration which might otherwise have dislodged the luminal thrombus. His initially high rate of embolisation on day 5 settled rapidly with the high dose dextran and a check duplex scan at 30 days showed no evidence of any residual stenosis or thrombus.

In summary, until there is a more effective method for identifying those at highest risk of suffering a postoperative carotid thrombosis it would seem reasonable to monitor all patients for 2–3 h post-operatively with TCD. The few, perhaps 5% with sustained embolisation will require dextran therapy the dose of which can then be modified according to the embolus count. Hopefully in the future it may be possible to modify the preoperative antiplatelet therapy in these patients so that the need for post-operative monitoring is rendered obsolete.

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