Warfarin treatment and migraine

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Summary: A patient suffering from migraine, whose symptoms were abolished by warfarin therapy, is reported. Warfarin was prescribed for deep vein thrombosis and the frequency of the patient's headache improved remarkably during the anticoagulant therapy. Because of the unusual nature of the response to anticoagulant therapy, warfarin was reintroduced on a double blind (versus placebo) basis and once again abolished the headaches.

Introduction

Sporadic case reports^{1,2} in the literature have suggested the disappearance of migrainous headaches with anticoagulant therapy. The mechanism of action of warfarin in vascular headache is unclear, however, studies have shown increased platelet aggregation and hypercoagulable plasma in patients with migraine.^{3–5} We report the case of a 71 year old woman whose migrainous headaches were abolished with warfarin therapy for deep vein thrombosis.

Case report

A 71 year old lady, with a long-standing history of migraine and angina, was admitted to the acute medical ward with swelling of the left leg and thigh. The swelling appeared 3 days prior to the admission and was progressively increasing in size. She was a long-term sufferer of migraine and many therapies had previously been tried. The headache most often was left sided and was frequently associated with vomiting and photophobia. Occasionally, vomiting relieved the headache. Paracetamol often was helpful during periods of headache; however, she occasionally had to resort to ergotamine tartrate tablet for relief of the headache. She continued to have migraine, 3–4 per week, despite prophylactic treatment with methysergide, which has been found to be the most effective of her many therapies.

A venogram confirmed the presence of thrombosis in the deep veins of the calf, femoral and iliac veins on the left side. A computerized tomographic

scan of the abdomen excluded the presence of any retroperitoneal fibrosis as a cause of the venous obstruction. The international normalized ratio (INR), clotting time, routine biochemical tests, white cell count, haemoglobin and the platelets were within normal limits.

She was commenced on warfarin sodium and was discharged home on a dose of 6 mg daily. On regular follow-up in the anticoagulant clinic, the INR was maintained between 2 and 3. When she was seen in the outpatient 2 months later, the venous thrombosis had cleared. She was pleased to report that she had noticed complete disappearance of migrainous headaches after prescription of the anticoagulant medication and had been able to discontinue the methysergide. She continued to be headache free when the warfarin was discontinued at 6 months. Two weeks later, her migraine had recurred, requiring prescription of methysergide.

It was thereafter decided to perform a double-blind placebo trial using a fixed warfarin dose (6 mg daily), as her anticoagulation was satisfactorily stable at this dosage during therapy for the deep vein thrombosis. The pharmacy kindly organized the trial and supplied the dummy warfarin tablets. Each phase ran for eight weeks and the patient attended at weekly intervals, during both phases of treatment to measure the INR. There was no change in dosage, either in the active or placebo phase of treatment. During the placebo phase, she continued to get migrainous headaches two to three times per week, but her headaches completely disappeared during the active phase of treatment. During this period, her INR remained between 2 and 3 (Table I). The dose was later reduced gradually and she continued to be asymptomatic on 3 mg of warfarin when the INR was between 1 and 1.2.

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Accepted: 18 June 1993

Table I Diary card of the patient showing the international normalized ratio (INR) and the frequency of migrainous headaches during the active (6 mg of warfarin daily) and placebo phases of treatment

Week	Active phase		Placebo phase	
	INR	Headaches/week	INR	Headaches/week
1	2.3	1	1.0	2
2	2.9	0	1.0	3
3	2.8	0	1.0	3
4	2.0	0	1.0	4
5	2.6	0	1.0	2
6	2.4	0	1.0	3
7	2.6	0	1.0	3
8	2.8	0	1.0	3

Discussion

A review has revealed similar case reports in which, migrainous headaches have responded to anticoagulant therapy.^{1,2} Thonnard-Neumann has reported the effectiveness of intravenous and aerosol heparin in patients with vascular headache.⁶ The migraine index was reduced by

86% in those treated with heparin aerosol and by 75% in those treated with intravenous heparin. The hypothesis put forward to explain this effect is that patients with migraine have less native heparin and fewer basophil leucocytes, and that the intravenous or aerosol heparin increases the amount of uroheparin to normal values. The heparin is thought to bind the vasoactive mediators or compete with them for the tissue binding sites.

The platelets of migrainous patients have a greater tendency to aggregate^{4,5} and during the headache phase show increased adhesiveness. Some patients with migraine have been shown to have hypercoagulable plasma.⁶ There have been isolated reports to suggest a decreased anticoagulant sensitivity after migrainous attacks,⁷ however it is not clear whether this phenomenon is due to increase in the blood levels of vitamin K-dependent clotting factors. The mechanism behind the reduction of migrainous headaches during warfarin treatment on our patient is unclear, however, the dramatic response leads one to suggest that in the very resistant patient, anticoagulants may be an alternative therapy.

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