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ORIGINAL ARTICLE

Novel Use of Thalidomide in Recurrent Gastrointestinal Tract Bleeding in Patients with Left Ventricular Assist Devices: A Case Series

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Background Bleeding is an important and common complication of left ventricular assist devices (LVADs). One of the common causes of gastrointestinal bleeding is arteriovenous malformations. However, the source of bleeding is often hard to identify. Thalidomide is efficacious in treatment of gastrointestinal (GI) bleeding in non-LVAD patients. We report our experience of the use of thalidomide in the treatment of GI bleeding in four patients with LVAD.

Method and Results Four patients who had recurrent GI bleeding from May 2009 to December 2014 were started on thalidomide. All of them responded to treatment and had no further gastrointestinal bleeding while on thalidomide. One patient developed constipation, requiring thalidomide to be stopped. Another patient developed symptomatic neuropathy, that resolved with reduction of dosage.

Conclusion Thalidomide appears safe and efficacious in LVAD patients with recurrent gastrointestinal bleeding.

Keywords Thalidomide • Gastrointestinal haemorrhage • Ventricular Assist Devices

Introduction

Q2 Recent advances in medical and device therapies in heart failure have improved the survival of patients with heart failure. In spite of this, a significant proportion of patients will continue to develop symptoms refractory to treatment, leading to the increasing use of left ventricular assist devices (LVADs).

One of the most important complications of LVAD is that of gastrointestinal (GI) bleeding. This may be a direct consequence of the anticoagulation therapy required in these patients, or a result of disorder of the coagulation system as a result of LVAD therapy [1]. It is usually difficult to identify the source of bleeding in most LVAD patients and the success of conventional therapy for GI bleeding in these patients remains unsatisfactory for many of these cases [2].

The novel use of thalidomide for the treatment of GI bleeding in non-LVAD patients has been found to be efficacious [3]. Its potential use in LVAD patients was first described only recently [4]. We report our experience on

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the use of thalidomide in the treatment of GI bleeding in four patients.

Case Series

Methods

All patients on LVAD support at our centre routinely receive aspirin 100 mg and warfarin (titrated to an International Normalised Ratio (INR) of 2.0 to 2.5 for HeartMate II and 2.5 to 3.0 for HeartWare) as their anticoagulation therapy daily. From May 2009 to December 2014, out of the 52 patients who received continuous flow LVADs in our centre, 8 patients developed gastrointestinal bleeding (0.0842 cases per patient year). As per protocol, both aspirin and warfarin are stopped whenever patients present with significant bleeding episodes, and resumed progressively once bleeding is resolved after conventional therapy. All the patients would undergo endoscopy to evaluate the cause of bleeding. Subsequent investigations are guided by the nature of their presentation and managed together with the gastroenterologists. Despite this workflow, 4 patients had recurrent bleeding episodes, prompting the use of thalidomide for their treatment. These patients were offered thalidomide as an alternative option as they still required multiple blood transfusions despite conventional treatment.

Results

Patient 1

A 66-year-old Chinese man with a HeartMate II (Thoractec, Pleasanton, CA) LVAD implanted for ischaemic cardiomyopathy presented with fresh per rectal bleeding on postoperative day (POD) 52. His INR on admission was 2.13 and his haemoglobin was 7.6 g/dl. An oesophagogastroduodenoscopy (OGD) was normal while colonoscopy demonstrated stale blood in the large intestines. Further bleeding episodes prompted an urgent computed tomography (CT) mesenteric angiogram, which could not identify the source of bleeding. A repeat colonoscopy subsequently found ischaemic colitis with ulceration. Despite repeat colonoscopy showing healing of the ulcer and colitis, he continued to experience intermittent bleeding per rectum. He was transfused nine units of blood. He was then started on thalidomide 50 mg nocte.

Thalidomide was stopped after two months, as his symptoms seemed to have abated. Unfortunately, bleeding recurred following the cessation of the drug, necessitating the recommencement of thalidomide. The patient has not had further episodes of bleeding for the subsequent eight months of follow-up. However, he developed symptomatic neuropathy, which resolved as we changed the dose of thalidomide to 50 mg every other night.

Patient 2

A 52-year-old Chinese man who had a HeartWare™ (HeartWare International, Framingham, MA) HVAD implanted for cardiogenic shock after emergency coronary artery bypass surgery. He developed fresh per rectal bleeding on POD 17. His INR then was 2.2 and his haemoglobin was 7.4 g/dL. OGD and colonoscopy did not show any obvious source of bleeding. His haemoglobin level continued to decline in spite of no further overt bleeding episodes. He required a total of seven units of blood to be transfused. Thalidomide 50 mg nocte was started with subsequent stabilisation of his haemoglobin level for the next three months. The patient experienced significant constipation and requested that thalidomide be stopped. There were no further episodes of bleeding for seven months as at the time of reporting.

Patient 3

A 67-year-old Chinese gentleman had HeartMate II LVAD implanted for non-ischaemic cardiomyopathy. He presented with melena on POD 57. His INR was 2.5 and his haemoglobin was 7.5 g/dL. He was extensively investigated with OGD, colonoscopy, CT enterography and tagged red blood cells scan which did not yield any positive results. He required transfusion of 13 units of blood. Thalidomide 50 mg nocte was started and maintained for eight months with no recurrence of bleeding.

Patient 4

A 55-year-old Indian man who underwent HeartMate II LVAD implantation for advanced ischaemic heart failure, presented with melena two months after surgery, requiring multiple blood transfusions. His INR was 2.2 OGD and his haemoglobin was 5.5 g/dL. Colonoscopy and mesenteric angiography were inconclusive. Capsule endoscopy revealed active bleeding in the jejunum, prompting further investigation with double balloon enteroscopy. This revealed a 5 mm bleeding ulcer in the jejunum, which was successfully clipped. Two months after resumption of warfarin, he was readmitted with melena. Double balloon enteroscopy revealed multiple jejunal mucosal ulcers, which were again clipped. He was transfused eight units of blood.

Thalidomide 50 mg nocte was started after a third episode of malena three months later. This resulted in a resolution of his bleeding. An attempt was made to reduce the dose to every other day three months later, but this resulted in a recurrence of the bleeding. On resumption of the original daily dose of thalidomide, he did not have further bleeding for the next 23 months.

Discussion

Bleeding remains a major complication of patients implanted with LVADs [5]. Besides the bleeding risks posed by antiplatelets and anticoagulation, other mechanisms or factors related to the interaction of the LVAD and the cardiovascular system have been proposed. In 1958, it was first noted by Heyde that there was high incidence of GI bleeding in patients with aortic stenosis [6]. There are two mechanisms that have been proposed that could have contributed to this

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