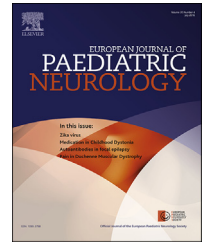




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Original article

Case series: Use of Glyceryl Trinitrate patches to improve peripheral circulation in children with severe neurodisability

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ABSTRACT

Aim: Evaluation of topical Glyceryl trinitrate as a therapeutic option to improve peripheral circulation in 16 children with severe complex neurodisability, poor capillary return and signs of vascular insufficiency, including discomfort.

Methods: If insufficient improvement in capillary return was obtained using conservative measures, a 5 mg GTN patch was placed each day on the front of the tibia of each leg. Children were reviewed clinically for up to 12 months of treatment. Distal limb comfort was measured using a Likert scale, either patient or carer reported. Standardised capillary refill time was assessed at each clinical review.

Results: Use of the patches led to improved capillary refill time and parent/patient reported comfort in all children. Healing of skin ulcers in lower limbs after application of the patch was also noted. There was universal parent/patient satisfaction with use of the patch. One child with Aicardi Goutieres syndrome had a skin reaction with prolonged use and minor adverse effects were reported in 4 others but this did not result in discontinuation of treatment.

Summary: GTN patches were relatively well tolerated in this group of children. We suggest that use of GTN patches be considered for children with severe neurodisability and poor peripheral circulation causing discomfort. GTN patches may also have a role in healing of persistent skin ulcers for these children.

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What this paper adds

- Highlights problem of recognition and management of vascular insufficiency, poor peripheral circulation and vascular discomfort in non-ambulant children and young people.
- In severe cases 5 mg GTN patches were relatively well tolerated and provided good efficacy with regards to improved capillary refill and comfort and, when present, healing of chronic superficial ulcers.

1. Introduction

Decreased peripheral perfusion in non-ambulant children is poorly reported but is regularly seen in clinical practice.^{1,2} Parents or carers may mention cold extremities as a concern to clinicians but this can often go untreated.³ This poor perfusion can be associated with ulceration around the foot and ankle as well as discomfort. Reasons for these difficulties may include secondary structural deformities, abnormal posture and biomechanics impairing the arterial blood supply, reduced venous and lymphatic drainage related to inactivity of lower limb muscles and/or altered autonomic nervous system control.

The pattern of related discomfort in non-ambulant or non-communicative individuals with vascular insufficiency is poorly understood. In adults this is characterized by a number of signs in the lower limb – pain at rest, which is increased by exercise, pallor, coldness, oedema, poor pulses, numbness, poor or reduced healing and a tendency to ulceration.⁴

Clinical assessment of the degree of vascular insufficiency includes measurement of the peripheral capillary refill time (CRT). This measures the time for colour to return from pale to pink in an area of skin after 5 s of firm pressure is applied by the clinician's finger over the dorsum of the foot of the affected limb.⁵ Normal CRT in the paediatric population is usually considered to be less than 2 s.⁶ Peripheral CRT is potentially affected by multiple factors including age, infection, medication, ambient temperature and reduced circulating volume as well as vascular insufficiency.⁷

Initial management for poor vascular return includes ensuring postural equipment is not physically compromising arterial flow or venous return and optimising both body and limb temperature. Warm footwear is vital, including the use of 9–12% silver socks as outlined by the Raynaud's Association.⁸ If these factors provide insufficient benefit Nifedipine is the only medicine licensed to treat Raynaud's phenomenon but the use of sustained release transdermal Glyceryl Trinitrate has been widely explored as another treatment option.⁹

Glyceryl trinitrate (GTN) is converted by the human body to nitric oxide, a potent vasodilator. Peripheral vasodilatation results in increased blood flow therefore reducing vascular insufficiency. It is also thought that there are direct anti-inflammatory effects, potentiating pain relief.¹⁰ GTN sublingual spray and/or patches also have widespread use to improve vascular return in the elderly or those with diabetic neuropathy.^{11,12} Reported systemic adverse effects of GTN include headache, dizziness, tachycardia, hypotension and

drowsiness. GTN can be administered transdermally as a topical adhesive patch, which is easily removed if adverse events occur. This route of administration may be more acceptable than oral medications to some children.

A UK study of the use of GTN patches in children with Raynaud's phenomenon showed this to be a safe, tolerable and effective treatment in relieving symptoms related to poor peripheral perfusion.¹³ We present a case series of 16 children and young people with severe neurodisability, poor peripheral perfusion and signs of vascular insufficiency in the lower limb, including presumed discomfort, treated successfully with GTN patches.

2. Population and method

Children and adolescents with severe physical neurodisability were referred to a specialist Complex Neurodisability regional service for evaluation of management including co-morbidity. From January 2015 to March 2016, of the 148 new patients seen, 27 presented with clinically severe poor peripheral circulation evaluated as a capillary refill time (CRT) of >10 s.

Initial simple measures to manage this were attempted. These included review of postural equipment to ensure no pressure points on arterial flow and vascular return; warming of lower limbs and feet using devices such as heat pads, sheep-skin lined boots and/or the use of heat retentive 9–12% silver socks as recommended by the Raynaud's Association. These improved the situation in 11/27. However despite using these measures for several months, 16 continued to have a CRT of over 12 s with or without obvious discomfort. 5 patients also had an area of chronic, poorly healing ulceration for over two months on the distal lower limb. These were then considered for further therapeutic intervention (m9:f7).

Of this group 13 CYP had severe Cerebral Palsy, five of whom were non-verbal, 11 were GMFCS V and 2 were GMFCS IV¹⁴; 1 was a non-verbal girl with Rett's syndrome, 1 boy had Pelizaeus-Merzbacher syndrome and 1 girl had Aicardi Goutieres (SAMHD-1). None of the children was known to have any underlying primary cardiovascular pathology. Their notes were checked to ensure lack of previous Cardiac history and they were individually discussed with the Regional Paediatric Cardiology team. Potential management with GTN was considered in the absence of known cardiovascular disease.

All children prior to treatment had a peripheral capillary refill time of more than 12 s (range 12–24 s). Presence and size of ulceration in the lower leg, ankle or foot was recorded. Five had chronic ulceration, greater than 0.5 cm in diameter, around the ankle or dorsal aspect of the foot, which had all been present for at least 8 weeks.

Potential vascular related ischaemic pain was considered on the basis of child's own description of discomfort in feet and lower limbs/restless legs, or parent report of pain behaviours. In the non-verbal children, in order to help focus on potential causes of discomfort, the primary carer completed a baseline Paediatric Pain Profile. A ten point Likert scale¹⁵ was then used to establish the baseline level for initial comfort and therapeutic outcome. During the time of treatment, the management for other potential causes of discomfort related

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