Journal of Plastic, Reconstructive & Aesthetic Surgery (2009) **62**, 1503—1509

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

Clinical evaluation of a resorbable wrap-around implant as an alternative to nerve repair: A prospective, assessor-blinded, randomised clinical study of sensory, motor and functional recovery after peripheral nerve repair

Maria Åberg*, Christina Ljungberg, Ellenor Edin, Helena Millqvist, Erik Nordh, Anna Theorin, Giorgio Terenghi, Mikael Wiberg

Department of Hand & Plastic Surgery Umeå University SE-901 87 Umeå, Sweden

Received 10 January 2008; accepted 6 June 2008

KEYWORDS
Biodegradable polymeric nerve conduit;
Peripheral nerve repair;
Randomised clinical trial

Summary Peripheral nerve injures are common and often result in impaired functional recovery. The majority of injuries involve the arm and/or the hand. The traditional treatment for peripheral nerve injuries is repair by using microsurgical techniques, either by primary nerve suture or nerve graft, but research to find more successful methods that could improve recovery is ongoing. Tubulisation has been investigated by several authors and is suggested as an alternative to microsurgical techniques. The resorbable poly[(R)-3-hydroxybutyrate] (PHB) is one of the materials that has been previously tested experimentally. In this prospective, randomised, assessor-blinded clinical study, PHB was investigated as an alternative to epineural suturing in the treatment of peripheral nerve injuries at the wrist/forearm level of the arm. Twelve patients, with a complete, common, sharp injury of the median and/or ulnar nerve at the wrist/forearm level, were treated by either using PHB or microsurgical epineural end-to-end suturing. All patients were assessed using a battery of tests, including evaluation of functional, sensory and motor recovery by means of clinical, neurophysiological, morphological and physiological evaluations at 2 weeks and 3, 6, 9, 12 and 18 months after surgery. No adverse events or complications considered as product related were reported, and thus PHB can be regarded as a safe alternative for microsurgical epineural suturing. The majority of the methods in the test battery showed no significant differences between the treatment groups, but one should consider that the study involved a limited number of patients and a high variability was reported for the evaluating techniques. However, sensory recovery, according to the British Medical Research Council score and parts of the manual muscle test, suggested

* Corresponding author. Tel.: +46 31 776 3345; fax: +46 31 776 3010.
E-mail address: maria.aberg@astratech.com (M. Åberg).

doi:10.1016/j.bjps.2008.06.041

that treating with PHB may be advantageous as compared to epineural suturing. This, however, should be confirmed by large-scale efficacy studies.

Peripheral nerve injures are common and often result in impaired sensory and motor function.[1–4] Since the majority of injuries involves the upper extremity, the patient's ability to function adequately is affected.[1,5] The traditional treatment for peripheral nerve injuries is primary repair by using epineural microsurgical suturing techniques, either end-to-end or, when there is a nerve defect, by interpositional nerve grafts.[2,6,7] However, research is ongoing to find more successful methods that would improve recovery after a nerve injury and simplify the surgical procedure. For example, tubulisation or entubulation have been investigated by several authors and suggested as an alternative to microsurgical techniques.[8–16] The concept of tubulisation in general, and a wrap-around conduit in particular, minimises problems related to lacerated tissues, that is, suturing with correct alignment, scar tissue formation, adherence and mismatch of nerve fascicles. It is also known that trophic factors accumulate in a tube between the damaged nerve ends, supporting the survival of neurons and re-growth of nerve fibres.[17,18] Repair using tubulisation has a long history[10,19,20] but is still not completely implemented in clinical practice. Non-biologic,[20] biologic,[21] and artificial materials have been investigated,[7,22] and luminal fillers have been introduced to further enhance nerve regeneration through conduits.[23] The most commonly reported artificial materials are different polymeric nerve conduits,[7,16,19,24,25] but the exact composition of the ideal nerve conduit is still not clear.[25] Poly[(R)-3-hydroxybutyrate] (PHB) is one of the bio-absorbable polymeric materials that has been extensively tested in several experimental studies as a wrap-around tubular implant for nerve repair.[26–35] It is a naturally occurring polymer produced by a range of organisms as an energy-storage medium and degraded by hydrolytic and enzymatic action, to the monomer D-(-)-3-hydroxybutyric acid, when implanted into the body.[36–38] The degradation product is a normal mammalian metabolite found in healthy adults in concentrations between 3 and 10 mg/l plasma.[38] The PHB material has previously been used as a pericardial substitute after coronary artery bypass grafting,[39–41] as buttressing to the staple line during lung volume-reduction surgery[42] and as wound dressing in the treatment of chronic leg ulcers.[43] Animal studies have reported the material to be useful as a wrap-around conduit in peripheral nerve injury as well, both with[26–31] or without[32–35] luminal fillers. This study was the first when PHB was tested in man for nerve repair, and the objectives were therefore to investigate whether PHB is a safe and clinically applicable alternative to epineural suturing and whether the experimental results of PHB could be confirmed in a clinical setting.

Methods

Patients and demographics

This study was conducted in accordance with the Helsinki declaration and approved by the local Research Ethics Committee at Umeå University (Um dnr 01-292). The study population included 12 patients with a complete median and/or ulnar nerve injury at the wrist/forearm level (Table 1). All patients were operated within 1 week after injury and reviewed at 2 weeks and 3, 6, 9, 12 and 18 months after surgery. The vast majority of injuries was sharp ulnar nerve division to the dominant hand. All patients had accompanying tendon injuries and the majority also had vascular injuries, although none of them needed revascularisation. Six of the patients were treated with PHB wrapped around the nerve ends in a tube-like fashion and sealed with fibrin glue, and six were treated with epineural end-to-end suturing using 9/0 non-absorbable sutures. Treatment allocation was decided at surgery using randomisation envelopes obtained from computerised randomisation with a block size of ten patients. All the patients gave their written, informed consent and fulfilled all the predefined eligibility criteria. Across treatment groups, no patients reported any medical and/or surgical history that was expected to affect the result of nerve regeneration.

Assessments

The selection of methods for the battery of tests was based on the model for quantitative documentation of the functional outcome after nerve injury and repair described by Rosén and Lundborg in 2003 and 2000 and Rosén in 1996.[44–46]

Table 1 Demography per treatment group

Population	PHB	Sutures
	$n = 6$	$n = 6$
Demographic characteristics		
Age (years)		
Mean	36	26
Median	34	25
Range	15–58	15–41
SD	17	10
Men (*n*)	5	6
Women (*n*)	1	–
Ulnar-nerve injury	4	5
Median-nerve injury	1	–
Ulnar- and median-nerve injury	1	1