Title

Woodcast vs Standard casting material for the immobilisation of non-operatively treated distal-radius fractures– A randomised parallel-group feasibility trial

Abstract

Background:
Distal radius fractures are the most common fracture sustained by the adult population. Most such fractures can be treated using cast immobilisation without the need for surgery. The aim of this study was to assess the feasibility of a definitive trial comparing the commonly used fibreglass cast immobilisation with an alternative product called Woodcast. Woodcast is a biodegradable casting material with theoretical benefits in terms of patient comfort as well as benefits to the environment.

Methods:
This **was a multicentre, two arm, open-label, parallel-group randomised controlled feasibility trial. Patients** with a fracture of the distal radius aged 16+ were recruited from four UK centres and randomised (1:1) to receive a Woodcast or fibreglass cast. Data was collected on participant recruitment and retention, clinical efficacy, safety and patient acceptability.

Results:
Over an eight month period, 833 patients were screened, 271 were found to be eligible and 120 were randomised. Patient reported outcome measures were available for 97% of participants at five weeks and 83% at three months. Clinical outcomes and patient acceptability was similar between the two interventions and no serious adverse events were reported in either intervention arm.

Conclusions:
Both interventions were deemed efficacious and safe in the cohort studied. This study showed that a definitive study comparing Woodcast and fibreglass was feasible in terms of patient recruitment and retention.

Clinical relevance:

- This feasibility study suggests that Woodcast is a safe alternative to fibreglass casting when used to support fractures of the distal radius. A larger study is required to definitively test clinical and cost effectiveness.

Registered with the ISRCTN registry: ISRCTN13706230
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1 INTRODUCTION

Hundreds of distal radial fractures are placed into cast every day in the UK. The ideal cast would be safe, efficacious, comfortable and low-cost. The search for this perfect immobilisation material has been ongoing

for many years, with many cast material adaptations and splint-devices being introduced to achieve these clinical and economic goals[1].

The initial utilisation of fibreglass material for upper limb fracture treatment in preference to Plaster-of-Paris was due to the perceived improvement in patient comfort. This change occurred despite the increased cost of fibreglass.

Fibreglass casts, applied below-elbow is a technique familiar to all those managing wrist fractures. The technique is simple, quick to perform and there are low numbers of reported complications. Fibreglass casts are also lightweight, water tolerable and made up of a strong material. Whilst efficacious and comfortable, there have been concerns raised about both the environmental and occupational safety of fibreglass products which are not bio-degradable, and release Isocyanates as a volatile by-product of the hardening process[2]. Isocyanates have been associated with contact dermatitis and occupational asthma[3, 4].

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Woodcast is a non-toxic, re-mouldable cast material. It is manufactured from wood and biodegradable plastic and can be applied without water or gloves. Used casts can be disposed of as either energy waste or bio-waste. The application of this cast requires the warming of a pre-fabricated sheet, and the moulding of this malleable sheet to the contour of the wrist. The material is non-toxic and can be reheated and remoulded if necessary, enabling the same material to be replied if a re-casting is necessary. However, there is limited data regarding the safety, efficacy and acceptability to patients of Woodcast as an alternative to fibreglass casting.

This randomised, multi-centre study compared Woodcast with fibreglass cast for patients with a dorsally displaced fracture of the distal radius in order to test the feasibility of a definitive trial. We report recruitment and follow-up rates, as well as adverse events and complications (safety), patient-reported functional outcome (efficacy) and patient-reported experience (patient acceptability).

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Patients and Methods:

This is a multicentre, two arm, randomised, parallel-group controlled feasibility trial conducted across four hospitals in the UK. Based on the UK trauma system, two of the hospitals are classified as major trauma centres (Oxford & Nottingham), and two are trauma units (Reading & Doncaster).

Participants were adult patients presenting to the fracture clinic with a fracture of the distal radius. Patients had previously been seen and treated in the Emergency Department with a temporary Plaster-of-Paris cast applied as per local-policy in the previous 24-72 hours.

Patients were eligible for inclusion into this study if:

- They had sustained a fracture of the distal radius within or equal to 3 cm of the radio-carpal joint.
- They were 16 years or older.
- They were able to give informed consent.
- Patients deemed suitable for non-operative treatment

Patients were excluded from this study if:

- The injury was more than one week old.
- The fracture was open.
- There was evidence that the patient would be unable to adhere to trial procedures or complete questionnaires, such as cognitive impairment.
- The patient sustained fractures to other areas of the body at the time they broke their wrist.

Consented participants were randomised (1:1) to receive either the standard cast (fibreglass) or Woodcast via a bespoke computer-based randomisation system run by the Oxford Clinical Trials Research Unit. Randomisation allocations used variable block sizes, stratified by study site and age group (<50 years, 50+ years); the lists were generated by a statistician and were concealed from researchers enrolling and assessing participants. The allocated cast was then applied as per standard hospital procedures. This was an open-label trial, and neither participants, clinicians nor outcome assessors were blinded.

This feasibility study was conducted to establish the rate of patient recruitment, participant retention rate and missing data at follow-up points in order to assess the feasibility of a definitive trial comparing fibreglass and Woodcast casts.

We recruited a convenience sample of 120 patients. The target sample size represents 25% of the sample size estimate required for a definitive trial estimated based on a clinically plausible minimally important clinical difference and standard deviation in the outcomes observed in similar patient populations. A sample size of 120 participants was also deemed appropriate in order to evaluate the feasibility to recruit consistently to a large and fast-paced trial. [5].

Outcomes were measured to assess the interventions in terms of safety, efficacy, and acceptability.

Safety was assessed by the enquiry into, and recording of, complications and serious adverse effects at each of the follow up appointments.

Efficacy was assessed by determining whether the fracture displaced to such a degree that further intervention was needed, the provision of pain relief, the return of wrist function after cast removal, and health related quality of life 3 months after randomisation.

Fracture displacement requiring intervention was assessed by patient report, and review of the clinical records at each of the review time points. In addition, at the conclusion of the study, radiographs obtained as part of routine clinical care were reviewed by an upper-limb and trauma fellowship trained consultant orthopaedic surgeon (SG) to identify any significant fracture displacement during the trial period.

Pain relief was measured through the administration of a weekly Visual Anaglogue Scale for pain (VASp). This scale records the average level of wrist pain experienced by the subject in the last week. The scale range was from 0 (no pain) to 10 (worst pain imaginable).

Post-treatment wrist function was determined using the Patient Rated Wrist Evaluation (PRWE) [6] and EQ5D-5L. The PRWE is a 15-item questionnaire, designed specifically for assessment of distal radial fractures and wrist injuries. Five questions relate to a patient's experience of pain and ten relate to function and disability. The total is scored between 0 and 100 (best score = 0 and worst score = 100). EQ5D-5L is a standardized instrument for measuring generic health status. *The maximum score for the EQ-5D-5L index is 1, which lower scores indicating worse health states.*

Acceptability was determined through assessments of the subjects experience of wearing the cast, with regards to comfort, weight, temperature and 'sweatiness', smell/odour and the level of support the cast provides. At the Week 5 visit, the patients were asked to provide a summary of their experiences for weeks 1-4 of their treatment period. The questionnaire used to assess these domains is provided in the supplementary material section.

Participants were sent weekly email or SMS messages, or received a phone call if they did not own a smart phone in order to obtain patient satisfaction ratings and pain levels (Weeks 1-4).

At three months post randomisation, final follow up questionnaires were administered via email or SMS message, or phone call if appropriate. Subjects were also asked questions about any complications they had encountered, and health resource use, since cast removal. A summary of the data collected is provided in table 1.

Ethics committee approval was awarded, and the trial was registered with the ISRCTN registry: ISRCTN13706230

Funding: This study was supported by an unrestricted research grant from Onbone Oy. The grant providers played no part in data collection, analysis or reporting.

2 RESULTS

120 eligible participants were recruited between June 2017 and March 2018. Details of the participants demographics and fracture descriptors can be found in Table 2. Of the eligible patients, 69% went on to be randomised, with the remaining 31% either declining participation into the trial or classified as 'missed'. Patients being 'missed' occurred either because they were not identified in clinic as being eligible (ie: noted respectively by research associates), clinical preference for a particular treatment making randomisation inappropriate or Woodcast treatment being unavailable in the clinic at that time due to staff familiarity with the product. 83% of the recruited participants had complete PROM data-sets at the final timepoint. The CONSORT flow diagram (Figure 1) shows the patient flow into and through the trial.

There were no serious safety concerns demonstrated in the participants in either treatment arm. No Serious Adverse Events (SAEs) were reported in this trial period. Eight minor complications were recorded in 8 separate participants, 7 (88%) of those occurred in the Woodcast treatment arm, and the majority of these minor complications related to symptoms of skin irritation. A complete list of minor complications is provided in Table 4.

Efficacy data for analgesic effect and post-treatment outcomes (PRWE) are presented in Figure 2 and Table 3. Radiographs at 5 weeks were available for 23 participants (19% of the trial population). In total, fracture displacement was found in two participants; one in each in treatment arm. Whilst relatively little data was available for the assessment of fracture displacement, no patient in the study required further intervention for loss of fracture position .

Health related quality of life assessment, performed by EQ-5D-5L at baseline or at 3 months after fracture, are shown in Table 3.

The acceptability of the interventions in with regards to comfort, weight, temperature and 'sweatiness', smell/odour and the level of support the cast provides appeared similar in all domains (Figure 3).

DISCUSSION

Feasibility studies are conducted to answer the question "can the study be done?". In this study, we have shown that a large definitive trial comparing fibre glass casts and Woodcast casts in the treatment of adult wrist fractures is possible. We have shown that we can recruit sufficient numbers of participants to such a trial (69% of eligible patients), and can obtain acceptable rates of follow-up data at 3 months (83%).

The two most common reasons identified for in-eligibility to recruit were the decision to treat the fracture operatively, and patient age <16. The exclusion of those aged <16 should be taking into account in any future trial design but it may remain appropriate to exclude these patients depending on the clinical question and its applicabiltiy to children.

The safety profile presented here shows no concerns regarding serious adverse incidents however we did observe more minor complications in the Woodcast treatment arm. The vast majority of these minor complications related to symptoms of skin irritation. This may be due to inexperience of fracture clinic technicians using the Woodcast application, or may represent a specific risk of Woodcast treatment. Any future trial should specifically aim to identify and quantify skin irritation in the treatment arms. In addition to monitoring for other adverse incidents.

In the assessment of efficacy, we aimed to investigate fracture displacement, pain relief and post-treatment return to function. One criticism of the trial may be that there is relatively little data on fracture displacement quantification to compare between the two study groups. This data was reliant on radiographs being taken at the 5 week follow-up assessment. During this study, radiographs at cast removal were not standard practice, and only performed if clinically indicated. This practice is in line with recent best practice guidance in the UK (**https://www.bssh.ac.uk/professionals/management_of_distal_radial_fractures.aspx**). Radiographs at 5 weeks were available for 23 participants (19% of the trial population). Our opinion is that the key indicator or efficacy in relation to fracture stability is that no patients in the study required further intervention for loss of position of the fracture. As such, this aspect of treatment efficacy appeared acceptable and comparable in the two groups.

Feasibility studies, by design, do not provide definitive, statisitically robust answers to questions of comparison between two interventions and caution should therefore be applied in interpreting feasibility study outputs. However, while the sample had insufficient power for statistical comparison of efficacy, the observed values for pain-experienced and post-treatment return to function (PRWE at 3 months) appear very similar between each group. Any future trial would probably be best conducted with a non-inferiority design in light of this observation.

In the remit of this feasibility study, we have performed sample size calculations for a definitive study. Assuming this was a non-inferiority study with a non-inferiority margin of 6 points on the PRWE, then based on the data collected during this feasibility study and using a standard deviation of 22 as observed

in the Fibreglass arm at three months post randomisation, a one-sided significant level of 2.5% and 90% power, 710 participants would be required, allowing for up to 20% loss-to-follow-up.

During the trial process, it was highlighted by some of the clinicians involved that an additional relevant intervention for comparison when treating minimally-displaced fractures may be a simple 'off the shelf' splint. If this comparative arm were added to a definitive trial then the total sample size (including loss to follow-up) would be 1065 assuming pairwise comparisons, and no adjustments for multiple testing were made.

Whilst it health-economics data was not collected or presented as part of this feasibility study, it is recognised that this would form an important component of any definitive study. Future work should record and report costs and resource-use in order to compare the two interventions in this regard.

This study confirms that a definitive trial comparing different forms of casting/splinting of adult distal radial fractures is feasible. The safety and efficacy data collected in this study appears similar between the two interventions. Any definitive study will need either 710 (2-arm) or 1065 (3-arm) participants, and the importance of collecting and reporting health economic data within a definitive study should be recognised.

Table 3 Patient reported outcome results at 3 months post randomisation

	Fibreglass[4] (n=48)	Woodcast[4] (n=51)
PRWE total score[1]	29 (22)	30 (21)
PRWE pain subscale[2]	16 (12)	15 (10)
PRWE function subscale[2]	13 (12)	15 (12)
EQ-5D-5L index[3]	0.758 (0.188)	0.734 (0.234)
EQ-5D VAS[1]	75 (19)	73 (22)

Means (standard deviations) are provided
[1]Scores range from 0-100, which higher scores indicting better health outcomes.
[2]Scores range from 0-50, which higher scores indicting better health outcomes.
[3]The maximum score for the EQ-5D-5L index is 1, which lower scores indicting worse health states.
[4]Mean (standard deviation) values presented

Table 4 Minor complications reported, by treatment

	Woodcast (N=60)	Fibreglass (N=60)	Total (N=120)
Straps falling off, requiring additional visit	1 (2%)	0	1 (1%)
Skin Irritation	5	1 (2%)	6 (5%)

Pain requiring cast change	1 (2%)	0	1 (1%)
Total number of complications	7 (12%)	1 (2%)	8 (7%)

Note: only one event was reported per participant

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