A randomised controlled trial of treatment for post-stroke homonymous hemianopia: screening and recruitment.

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Abstract

Purpose: We report the screening process and recruitment figures for the VISION trial: Visual Impairment in Stroke; Intervention Or Not.

Methods: Prospective, randomised, single-blinded, three-arm controlled trial in fourteen UK acute hospital stroke units. Stroke teams identified stroke survivors suspected as having homonymous hemianopia. Interventions included Fresnel prisms versus visual search training versus standard care (information only). Primary outcome was change in visual field assessment from baseline to 26 weeks. Secondary measures included change in quality of life questionnaires.

Results: Recruitment opened in May 2011. 1171 patients were screened by the local PIs. 178 of 1171 patients (15.2%) were eligible for recruitment: 87 patients (7.4%) provided consent and were recruited. 91 patients (7.8%) did not provide consent. 993 of 1171 patients (84.8%) failed to meet the eligibility criteria. Almost half were excluded due to complete/partial recovery of hemianopia (43.6%; n=511).

Conclusions: The most common ineligibility reason was recovery of hemianopia. When designing future trials in this area, changes in eligibility criteria/outcome selection to allow more patients to be recruited should be considered, e.g. less stringent levels of visual acuity/refractive error. Alternative outcomes measurable in the home environment, rather than requiring hospital attendance for follow-up, could facilitate increased recruitment.

Introduction

Homonymous hemianopia is loss of half of the field of vision to the right or left side. It may be complete, in which total field loss occurs to one side from the vertical midline outwards, or may be partial, in which part of the field remains either centrally or in the periphery (temporal, superior or inferior remnant) [1].

Homonymous hemianopia is a common sequela to stroke and is reported in up to 57% acutely post stroke onset [2-5]. If a patient recovers, this is usually by 3 months and may be full, with a return of normal visual fields in up to 44%, or partial recovery in up to 72% [2,6-12]]. Where homonymous hemianopia persists it has considerable impact to daily life. Studies that have addressed this impact report a loss of confidence, increased

accidents and collisions, reading difficulties, navigation issues, loss of driving, and issues with isolation [2,13-15]. A variety of treatment options have been reported for homonymous hemianopia and these are summarised in a recent Cochrane systematic review [16]. However, there remains limited evidence for the efficacy of treatment options. Our pilot trial sought to compare two inexpensive treatment options (prism therapy and visual search training) with a control group of standard care [17]. This paper reports the VISION trial (Visual Impairment in Stroke; Intervention Or Not) screening data and final recruitment numbers.

Methods

The VISION trial was conducted as a multi-centre three arm pilot randomised controlled trial with independent assessment of results across 14 hospitals. For the full trial protocol please see reference 17. Interventions were: Fresnel prisms (arm a); visual search training (arm b) and standard care (information sheets only) (arm c).

Setting

The trial was undertaken in hospital in- and out-patient, and primary care rehabilitation settings.

Target population

Patients were identified in the acute phase following admission to hospital with a stroke (at 2 weeks post stroke onset).

Inclusion criteria

Participants were 18 years of age and older, and had best corrected visual acuity of ≥6/18 in either eye, homonymous hemianopia and refractive error within ±5D. Measurements of vision were by orthoptic assessment.

Exclusion criteria

Participants were excluded if they were: unable to consent due to severe cognitive impairment; unwilling to participate in the study; had ocular motility impairment and visual inattention in addition to the visual field impairment (as assessed by the orthoptist); had pre-existent visual field impairment.

Screening

The stroke team within participating stroke units identified stroke survivors suspected of having a homonymous hemianopia. The stroke research nurse listed details of these patients on the trial screening log. The Principal Investigator for the trial was an orthoptist specialising in the assessment of stroke-related visual impairment who arranged assessment of these patients

Recruitment

Patients listed on the trial screening log were contacted either in person if an in-patient, or via telephone if discharged. Patients were invited for eye assessment, conducted by the PI in the eye clinic. At assessment, patients who did not meet the inclusion criteria were excluded and reasons for exclusion were recorded. All patients meeting the inclusion criteria were invited to participate in the trial. Patients who declined to participate were invited to provide a reason, although PIs made it clear that this was not required; any reasons provided were recorded..

Results

Recruitment period

The VISION trial opened to recruitment in May 2011. During the recruitment period fifteen NHS Trusts were opened to recruitment; five of these opened in the first months. Recruitment was slow and the number of recruiting sites was subsequently increased. The month and year when each site opened to recruitment is given in Table 1. Time taken to obtain Research and Development unit approvals locally combined with completion of trial setup paperwork by local research teams ranged from 1 to 21 months. One site opened in the final month of recruitment period and therefore did not contribute to screening and so is not listed in the results tables.

Screening data

Total screening and recruitment numbers across 14 sites are provided in Table 1. A total of 1171 patients were identified by the stroke team as having suspected homonymous hemianopia and were recorded on the trial screening log. Figure 1 shows the flow of eligibility.

In total 993 patients (993/1171, 84.8%) failed to meet the eligibility criteria or could not be recruited to the trial for a variety of other Reasons; Table 2 provides a breakdown of these. The most common reason was failing to meet the criteria of a stable homonymous hemianopia (present no less than 2 weeks and no longer than 26 weeks post stroke) because of full or partial recovery in 511 patients (511/1171, 43.6%). Coexistent ocular motility impairment and/or presence of visual inattention was a failed criteria by 161 patients (161/1171, 13.7%) as was failure to achieve best corrected distance visual acuity of 0.5 logMAR or better in 97 patients (97/1171, 8.3%). Pre-existent visual field loss ruled out recruitment of 46 patients (46/1171, 3.9%) and 117 patients (117/1171, 10.0%) could not be recruited to the trial because they were unable to consent or could not understand the trial information because of cognitive or communication impairments.

Recruitment data

In total 178 patients (178/1171, 15.2%) were eligible for recruitment and 87 of these (87/178, 48.9%) provided consent and were subsequently recruited to the trial. Reasons eligible patients declined consent are outlined in Table 2. Ninety-one patients did not provide consent (91/178, 51.1%), of which 52 (52/91, 57.1%) did not disclose a reason. Of the patients who did provide a reason, twenty-five patients (25/91, 27.5%) did not want to attend the follow-up appointments required for the trial and eight (8/91, 8.8%) did not want to be randomly assigned.

The overall proportion of screenings resulting in recruitment was 7.4% (87/1171). This proportion varied across the 14 sites from 1.26% (3/238) to 20% (5/25) with table 1 providing more details. Time open to recruitment varied across sites with a median of 17.5 months and range of 7 to 28 months (table 1) with lower recruitment rates in sites open longest.

Discussion

The recruitment phase of the VISION trial commenced in May 2011 and ceased in August 2013. During this period 1171 patients were screened of which less than 10% were randomised (n=87). Recruitment was initially slow and formal feedback from the

PIs during an end-of-trial investigator meeting suggests this may be due partly to lack of familiarity with the trial and research process.

Research is relatively new in this field. Staff, who are new to research trials, must learn new processes (as was the case in our trial). For this trial a local orthoptist was the principal investigator at each recruitment site. Many of our PIs had participated in previous observation studies but this was their first PI role in a trial.

There was also a learning curve for the stroke research nurses. Although experienced at recruiting, for many they had to acquire knowledge of the various visual conditions that could co-exist with homonymous hemianopia to aid identification of suspected hemianopia. Continuous feedback and information were provided by the orthoptists to the stroke teams to facilitate an on-going update of knowledge of visual conditions, particularly for new staff with no prior vision experience. It was recognised that lack of knowledge and information could be a limitation in the identification of hemianopia by members of the stroke team. Sites opening to recruitment a year or longer after the initial sites possibly benefitted from the knowledge and experience passed on by the orthoptist PIs of the original sites. Consequently recruitment rate was generally higher for the later opening sites. These may be important lessons for future studies in this area.

Low recruitment numbers remained an issue through the first year of recruitment; there were fewer eligible patients than expected and smaller numbers of patients agreeing to take part. Slow and low numbers of recruitment to trials is well reported [18-21]. Barriers to trial participation include a lack of patient time, issues with their perceived importance of the trial, poor patient-clinician relationship and a lack of compatibility between the trial protocol and usual clinical practice [19]. Strategies to improve recruitment to trials have been advocated and include telephone reminders, participant opt-out versus opt-in options for trial contact and open designs [21].

We found a high number of patients who did not meet the trial inclusion criteria due to full or partial recovery of hemianopia but other reasons included; death prior to baseline assessment, further stroke, patients moved out of area or could/did not attend baseline assessment appointments. Patients who were eligible but who did not wish to consent to the trial often did not want to attend follow-up appointments, did not want to be

randomly assigned to a treatment group or be assigned to the control (no treatment) group, wanted to wait for natural recovery, did not wish to travel to the hospital for appointments (a requirement for outcome measures), did not anticipate any benefit to participating in the trial or their family did not wish them to participate.

Almost half (511/1171, 43.6%) of all screenings resulted in patients not being recruited for reasons related to recovery of hemianopia, which included either full recovery with return to normal visual field to the previously affected side, or partial recovery to less than one quadrant. The literature reports that up to 44% of individuals have full recovery of visual field and up to 72% have partial recovery although the extent of this recovery is not stated [2,6-12]. Our screening results show 43.6% full or partial recovery but of note, the partial recovery in our excluded cases was to less than a quadrant of visual field. This is a positive finding as a small visual field defect, particularly in the peripheral visual field, may not functionally impede an individual to anything near the extent of impact from complete homonymous hemianopia. This factor should be taken into consideration when planning future trials.

Of total screenings, 161 patients were excluded (161/1171, 13.7%) who had acquired eye movement deficits that prevented accurate horizontal gaze to the side of the hemianopia, for example horizontal gaze palsy. The reason for this is that treatment with visual search strategies utilised eye scanning exercises. These rely on the patient being able to make eye movements to look at different targets to the right and left sides of the exercise card. It was important to exclude eye movement deficits that might impede the process of doing the eye scanning exercises. Thus we propose this inclusion criterion should remain in future trials using visual search training.

Presence of high refractive error precluded the recruitment of only seven patients (7/1171, 0.6%). Formal quantitative perimetry of the peripheral visual field is typically done without glasses as the frames can impede the test by blocking the stimuli. Individuals with high refractive errors may therefore not detect stimuli if undertaking the test without their glasses. Thus they were excluded. The level of visual acuity was set at 0.5 logMAR or better level, as quantitative perimetry requires sufficient visual acuity to maintain adequate fixation of the central stable target during formal assessment. Ninety-seven patients (97/1171, 8.3%) did not meet this criterion. It is possible to increase the

visual acuity cut-off to a lower acuity level but not less than 6/60 Snellen or 1.0 logMAR level and future trials could consider this. This change in the inclusion criteria would allow a small increase in recruitment of patients but it would still be necessary to exclude those with visual acuity worse than 6/60 or 1.0 if formal perimetry remained an outcome measure.

A further consideration in relation to formal visual field assessment is that a number of patients could not participate because they did not wish to attend follow-up appointments or had transport difficulties so could not travel for appointments (35 patients, 3%). We required hospital attendance for follow-up appointments because formal visual field assessment was an outcome measurement. A consideration for future hemianopia trials is whether formal visual field perimetry is required as an outcome measure. If outcome measurements could be completed at home or community settings, recruitment may be improved. Furthermore, exclusion based on refractive error or level of visual acuity may not be necessary.

Conclusions

Of 1171 patients screened with possible hemianopia, we identified 178 eligible patients (15.2%) from which we recruited 87 patients, which represents 7.4% of the total screened patients and 48.9% of eligible patients. Just under half of patients screened could not be recruited because their hemianopia had fully or partially recovered which is a positive finding for stroke outcomes. It would be possible to recruit a small additional number of hemianopia patients with less stringent inclusion criteria for level of visual acuity and refractive error, and with varied outcome measurements not requiring formal hospital visits for perimetry or other quantitative assessments. Support for staff when screening and recruiting to trials, may promote improved recruitment rates across multi-centre trials. Consequently although we recruited fewer participants than we anticipated, our findings are important for the future planning of trials and studies for the care and treatment of patients with homonymous hemianopia.

Author contributions

FR, GB, RB, AD, MGF, SJ, CM, CN, AP, JR and CS conceived the study, participated in the design and coordination, and helped to draft the manuscript. EB, CD, CH and TS participated in the coordination and helped to draft the manuscript. MGF supervised the statistical analysis. EJC performed the statistical analysis, data monitoring, computed tables and figures and helped to draft the manuscript. EC participated in the coordination, data management and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing/Declaration of interests

This trial is funded by the UK Stroke Association, which includes salaries for EC. The sponsor (University of Liverpool Research Support Office) and funder (the Stroke Organisation) had no role in the study design, collection, management, analysis, interpretation of data, writing of the report; and the decision to submit the protocol for publication.

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Data sharing statement

There is no additional unpublished data in relation to the screening process for this trial. All data are held at the Clinical Trials Research Unit, University of Liverpool.

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Figure 1 Flow chart of recruitment figures

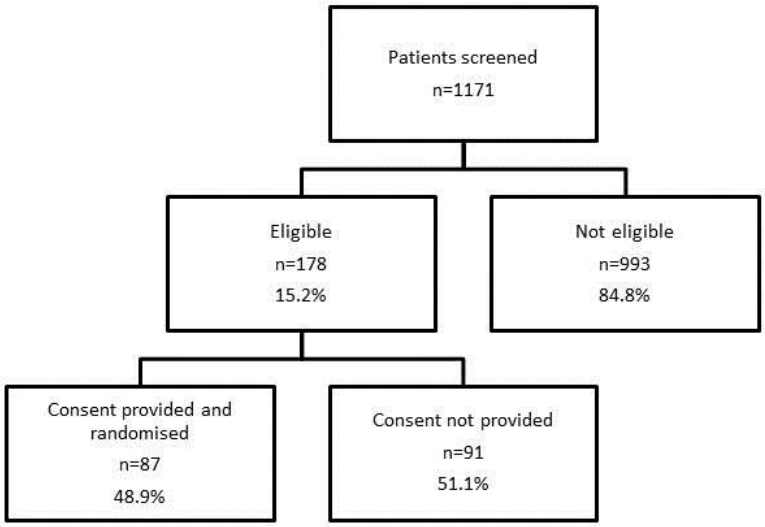

Table 1 Summary of site screening and recruitment

Site	Date site opened to recruitment	Months open to recruitment*	Number screened patients	Number ineligible patients	Number unwilling patients	Number eligible patients	Total patients recruited	Consent
1	May 2011	28	122	110	5	12	7	58%
2	May 2011	28	104	92	3	12	9	75%
3	May 2011	28	187	158	15	29	14	48%
4	May 2011	28	112	85	13	27	14	52%
5	August 2011	25	238	224	11	14	3	21%
6	March 2012	18	72	64	5	8	3	38%
7	March 2012	18	38	33	3	5	2	40%
8	April 2012	17	36	18	11	18	7	39%
9	April 2012	17	89	77	9	12	3	25%
10	May 2012	16	53	42	5	11	6	55%
11	June 2012	15	25	13	7	12	5	42%
12	November 2012	10	31	23	2	8	6	75%
13	January 2013	8	22	18	2	4	2	50%
14	February 2013	7	42	36	0	6	6	100%
15	July 2013	2	NA	NA	NA	NA	NA	.

*Rounded up to nearest month

Table 2 Reasons for being ineligible for recruitment and not providing consent

Reason: ineligible	Total screenings	Proportion
Unstable hemianopia	511	43.6%
Ocular motility impairment and/or visual inattention	161	13.7%
Not able to consent / understand	117	10.0%
Visual acuity worse than 0.5 logMAR	97	8.3%
Pre-existent visual field impairment	46	3.9%
Died	33	2.8%
Moved/lived out of area	17	1.5%
Could not attend	22	1.9%
Did not attend	11	0.9%
Unable to contact patient	11	0.9%
Further stroke	8	0.7%
High refractive error	7	0.6%
Unable to read and understand English	3	0.3%
Further TIA (transient ischaemic attack)	2	0.2%
Does not have transport	2	0.2%
Not 18 years of age or older	2	0.2%
Other:	5	0.5%
No reason provided	2	0.2%
Total patients	993	84.8%

Reason: consent not provided	Total number	Proportion
Did not wish to provide reason	52	57.1%
Did not want to attend follow up visits	25	27.5%
Did not want to be randomly assigned treatment	8	8.8%
Did not want to be assigned to information only group	1	1.1%
Other reason: Terminal patient	1	1.1%
Other reason: Patient wishes to see if recovers before participating	1	1.1%
Other reason: Family did not want to participate	1	1.1%
Other reason: Patient wishes to have more time to decide	1	1.1%
Other reason: Patient does not see benefit in trial	1	1.1%
Other reason: Patient does not want to travel to appointments	1	1.1%
Total patients	91	100%

Other = Patient denied vision problem, Barrier nurse, Unable to be assessed by orthoptist, Patient having further treatment for migraine.