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Multidisciplinary care for Guillain-Barré syndrome

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***Background*. Guillain-Barré syndrome (GBS) can be a significant cause of new long-term disability, which is thought to be amenable to multidisciplinary care. However, the evidence base of its effectiveness is unclear.**

***Aim*. The aim of this systematic review is to assess the effectiveness of multidisciplinary care in adults with GBS, the types of approaches that are effective (setting, type, intensity) and the outcomes that are affected.**

***Methods*. The search strategy comprised: The Cochrane Neuromuscular Disease Group Specialized Register and the Cochrane Central Register of Controlled Trials; MEDLINE, EMBASE, AMED, PEDro, LILACS and CINAHL (up to May 2010). Selected studies included randomized and controlled clinical trials that compared multidisciplinary care in GBS with a control (routine local service, lower level of intervention); or studies that compared multidisciplinary care in different settings or at different levels of intensity of therapy. Best evidence synthesis was based on methodological quality. Three observational studies were also reported but they make limited contribution to evidence base synthesis.**

***Results*. No randomized or controlled clinical trials were identified. Evidence from three low-quality observational studies provide some support for improved disability in the short term (6 months) with high intensity rehabilitation; and for improved participation and quality of life.**

***Conclusion*. The gaps in existing research should not be interpreted as ineffectiveness of multidisciplinary care in GBS. Appropriate and methodologically robust study designs, responsive outcome measures; and more research in the setting, type and intensity of rehabilitation are needed.**

KEY WORDS: Guillain-Barre syndrome - Disability evaluation - Evidence-based medicine.

Guillain-Barré Syndrome (GBS) is an acute demyelinating polyradiculopathy due to inflammation of the peripheral nerves and nerve roots which usually causes severe motor deficits (symmetrical ascending paralysis), autonomic dysfunction and respiratory failure.[1-3] It has a reported male preponderance [4] and can occur at any age (usually older individuals, but common between ages 30 and 50 years). It has a worldwide annual incidence of 1-2 per 100 000 with no geographical clustering.[5,

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[6] In developed countries, GBS mortality has been reduced to two to three per cent but this is higher in the developing world.[7] Despite the low overall mortality associated with GBS and the generally favourable outcome- approximately 3% of patients may die of complications in the acute phase of GBS,[7] up to 25% require artificial ventilation (involvement of respiratory and bulbar muscles), and 20% may have residual permanent severe disability, with deficits in ambulation or require ventilator assistance 12 months later.[8]

GBS is recognised as a heterogeneous syndrome with several variant forms. The most common type of GBS is acute inflammatory demyelinating polyradiculoneuropathy. Axonal subtypes include acute motor axonal neuropathy and acute motor and sensory axonal neuropathy. Variants of GBS include Miller Fisher syndrome (cranial nerve involvement, ataxia) and acute pandysautonomia.[9] The progressive phase in GBS is limited to four weeks.[10] In 30% of patients, the disease course may be fulminating, with rapid progression requiring ventilatory support within a couple of days.[1] Autonomic dysfunction (sinus tachycardia or bradycardia, fluctuating hypertension or hypotension, flushing of the face, loss of or excessive sweating) occurs in 70% and is associated with sudden death.[3] A number of factors, including preceding diarrhoea, older age, rapid progression, disability at nadir and specific neurophysiological parameters have been associated with poor outcome.[11, 12] Recently, a more readily applicable clinical prognostic scoring system, the Erasmus GBS outcome score was developed to predict poor outcome (inability to walk independently at six months) based on three variables: age, preceding diarrhoea, and GBS disability score at two weeks.[13]

The longer term sequelae of GBS and their impact on everyday life are not yet fully understood. The impairment (weakness and sensory disturbance), disability and psychosocial and quality of life (QoL) effects (including work, leisure activities and social activities) can be prolonged. Studies show that psychosocial performance does not necessarily correlate with the severity of impairment in GBS, but may be explained by poor conditioning and fatigue.[14, 15] A recent study (N.=76) reported that despite good functional recovery up to 14 years post GBS (median 6 years, range 1-14), 16% continued to report moderate to extreme impact on work, family and social activities; and 22% reported ongoing substantial impact on mood, confidence and ability to live independently.[16] With improvements in medical treatments and decreased mortality rates, the emphasis is on provision of integrated care to GBS survivors over a longer time period, as these individuals are often young. Long-term management of psychological sequelae impacting activity and participation is important. It is hypothesized that this may be best done through multidisciplinary rehabilitative care, which is defined as a problem solving educational process delivering co-ordinated care with clearly identified goals within a specified time period, utilising at least two disciplines (medicine, physiotherapy, occupational therapy, other allied health professions); and targeted towards improvements at the level of activity (function) and /or participation (QoL, social reintegration, work).

The aim of this review was to assess the effective-

TABLE I.—*Levels of quality of individual studies.*

Judgement of risk of bias	Quality rating of study
Risk of bias of all domains low	High methodological quality = 'high quality study'
Unclear or high risk of bias for one or more domains	Low methodological quality = 'low quality study'
High risk of bias for most domains	Very low methodological quality = 'very low quality study'

TABLE II.—*Levels of quality of a body of evidence in the GRADE approach.*

Underlying methodology	Quality rating
Randomised trials; or double-upgraded observational studies.	High
Downgraded randomised trials; or upgraded observational studies.	Moderate
Double-downgraded randomised trials; or observational studies.	Low
Triple-downgraded randomised trials; or downgraded observational studies; or case series/case reports.	Very low

TABLE III.—*Characteristics of observational studies.*

Demir 2008 [18]	Methods	Case-controlled study
	Participants	N.=65 (Intervention N.=34, control N.=31) Inclusion: all patients admitted to a rehabilitation unit over a 5-year period who fulfilled the standard diagnostic criteria for Gullian Barre syndrome (GBS) Control participants were selected from among hospital workers and patients' relatives who did not have any major illness and were not taking any medication. Exclusion: age <18 years and atypical variants of GBS Turkey
	Interventions	Treatment: inpatient rehabilitation program - no further description provided Control: healthy controls - no intervention
	Outcomes	Limitation of activity <12 months - Functional Independence Measure (FIM) Quality of life <12 months - Nottingham Health Profile (NHP)
	Assessment timepoints	FIM - Admission, discharge and 6 months in intervention group only. NHP - 6 months only in all participants.
	Risk of bias	Adequate sequence generation: no Adequate allocation concealment: no Blinding: no. Whilst blinding of patients and therapists would not have been possible due to the nature of the study, outcome assessors could have been blinded. Incomplete outcome data addressed: no. Three patients did not complete participation (1 death and 2 unable to complete rehabilitation) but none were included in the analysis. Free of selective reporting: yes. Other bias: Study design - prospective cohort study. Intervention was not clearly described other than "inpatient rehabilitation". Neither duration of intervention nor type of rehabilitation stated. Also unclear if all the subjects in the intervention group received a similar program. Intervention and control groups were not comparable as control group consisted of healthy individuals not receiving any interventions. No rationale was given for choice of controls. FIM was not measured in control group, hence no comparison of functional measures between intervention and control groups. Baseline NHP was not collected for any of the participants. No sample size calculation performed.
Meythaler 1997 [19]	Methods	Retrospective cohort study
	Participants	n = 39 Inclusion: all patients admitted to a rehabilitation unit over a 3 year period who fulfilled the standard diagnostic criteria for GBS. Exclusion: patients not admitted directly from acute care; patients who had undergone previous inpatient rehabilitation. United States
	Interventions	Treatment: Individualised inpatient multidisciplinary rehabilitation program with 3 to 4 hours daily of physical and occupational therapy, and psychology and speech therapy if indicated.
	Outcomes	Limitation of activity < 12 months - Functional Independence Measure (FIM)
	Assessment time points	Baseline (admission to rehabilitation) and discharge from inpatient rehabilitation (26 SD ± 18.6 days from baseline).
	Risk of bias	Adequate sequence generation: no Adequate allocation concealment: no Blinding: no. Incomplete outcome data addressed: yes. All subjects fulfilling the inclusion criteria were included in the final analysis. Free of selective reporting: yes. Other bias: Study design: retrospective case review therefore subject to documentation bias No control group
Nicholas 2000 [20]	Methods	Retrospective cohort study
	Participants	N.=24 Inclusion criteria: all patients admitted to a rehabilitation unit over a 3 year period who fulfilled the standard diagnostic criteria for GBS Exclusion criteria: not provided U.K.
	Interventions	Intervention: Individualised inpatient multidisciplinary rehabilitation (consultant neurologist, clinical nurse specialist, two sessions of physiotherapy and one session of occupational therapy daily, and if required, speech pathology and psychology).
	Outcomes	Activity limitation <12 months - modified Barthel Index (BI), Functional Independence Measure (FIM) Quality of life <12 months - Environmental Status Scale (ESS), Handicap Assessment Scale (HAS)
	Assessment timepoints	Admission to and discharge from inpatient rehabilitation (48 ± 32 days)
	Risk of Bias	Adequate allocation concealment: no. Blinding: no. Incomplete outcome data addressed: yes. All subjects fulfilling the inclusion criteria were included in the final analysis. Free of selective reporting: yes. Other bias: Study design: retrospective case review therefore subject to documentation bias No control group

N.: total number; SD: Standard Deviation.

ness of organized multidisciplinary care (MDC) in adults with GBS, especially the types of approaches that are effective (settings, intensity) and the outcomes that are affected.

Materials and methods

The Cochrane Neuromuscular Disease Group methods search strategy identified all randomized (RCT) and controlled clinical trials (CCT) that compared MDC with routinely available local services or lower levels of intervention; or trials comparing interventions in different settings or at different levels of intensity. Studies of 'other designs' (such as observational studies) were included with the understanding that such studies could only be of limited contribution to the best evidence synthesis.

Four reviewers selected trials and rated their methodological quality independently. Assessment of risk of bias was performed according to the Cochrane Handbook of Systematic Reviews of Interventions (Chapter 8.5),[17] from the domains: sequence generation, allocation concealment, blinding of participants, therapists and outcome assessors, incomplete outcome data and selective outcome reporting (details are available in the full review). Quantitative analysis was not possible due to lack of studies identified and other clinical heterogeneity. Therefore qualitative synthesis of 'best evidence' was presented based on the GRADE approach to grading the quality of evidence, as described in the Cochrane Handbook for Systematic Reviews of Interventions (Tables I, II).[17] Subgroup analysis was not possible due to lack of studies.

Results

The literature search did not identify any RCTs or CCTs that compared MDC in GBS with either routinely available local services or lower levels of intervention; nor were there any trials that compared multidisciplinary types of care, or care in different settings or at different levels of intensity.

Three observational studies met the criteria for "other designs" [18-20] (Tables III, IV). These studies involved a total of 128 participants in three different countries (Turkey, United Kingdom and United States) and were conducted in inpatient rehabilitation settings. All studies were rated as 'very low quality' due to small numbers (between 24 and 65 participants), lack of methodological robustness, unsystematic clinical observations and presence of critical problems. For example, Demir (2008) [18] was a "case-controlled" study comparing outcomes of GBS patients at six months following rehabilitation with healthy controls. No rationale was given for choice of controls nor description of intervention other than "inpatient rehabilitation". Meythaler (1997) [19] and Nicholas (2000) [20] were retrospective cohort studies comparing outcomes at the start and end of a four to six-week, high-intensity, rehabilitation programme. All three studies demonstrated an improvement in disability from the time of inpatient rehabilitation admission to discharge in a timeframe of less than 12 months. In addition, one study [18] showed an improvement in disability at six-month follow-up after rehabilitation. Insufficient evidence was provided to examine improvement in QoL during or after rehabilitation. Nicholas (2000) [20] demonstrated a reduction in handicap but only half the patients in the already small study completed the measures. All three studies included patients with severe GBS with high levels of physical dependency, which limits the generalisation of the results to patients with less severe GBS.

Discussion

In the absence of methodologically robust trials, the 'best' evidence to date is limited and are based upon three 'very low quality' observational studies. These studies provide some support for improved disability and reduction in handicap (participation) in the short term (less than 6 months) with high intensity inpatient multidisciplinary rehabilitation.

This review highlighted a number of limitations in GBS studies. Findings are often inconclusive due to poor methodological rigour. In addition, adequate descriptions of the content of multidisciplinary care are often lacking. Difficulties in assimilation of data is further compounded by the diversity of outcome measures. Key areas such as cost-effectiveness of GBS care and neuropsychological sequaelae following GBS (such as mood and work-related issues) have yet to be addressed. Lack of longer-term follow up is also an issue. Hence, recommendations for future research include:

TABLE IV.—*Results of observational studies.*

Demir 2008 [18]	Statistical analysis	Wilcoxon matched-pairs signed-rank test, Mann-Whitney U test, Spearman analysis.
	Results	Activity limitation - There were improvements in reduction of disability as measured by Functional Independence Measure (FIM) gains (mean ± SD) from admission to discharge (33.2 ± 12.7, P=0.001) and also at 6 months after rehabilitation (20.9 ± 13.4, P=0.001). Gullian Barre syndrome (GBS) patients had poorer health-related quality of life at six months after rehabilitation compared with healthy controls. The scores of all of the Nottingham Health Profile (NHP) domains (intervention mean ± SD *vs.* control) were statistically significantly higher in the patients (physical mobility 51.8 ± 29.7 *vs.* 5.3 ± 5.6, energy 40.7 ± 35.8 *vs.* 9.2 ± 11.3, pain 20.5 ± 20.2 *vs.* 5.2 ± 11.4, sleep 38.9 ± 32.8 *vs.* 11.7 ± 20.3, social isolation 34.9 ± 32.8 *vs.* 5.2 ± 9.7 and emotional reactions 31.5 ± 23.7 *vs.* 9.5 ± 21.4, P < 0.001 for all domains). Functional scores both at discharge and at the six-month follow-up were highly related to the NHP scores (P<0.05 across all domains). In particular, the correlations between FIM scores and the energy level (r=-0.58 at discharge), physical mobility (r=-0.61 at discharge and r=-0.48 at 6 months) and emotional reaction (r=-0.41 at 6 months) domains of NHP were highly significant (P<0.01). Being a female, employment, mechanical ventilation, a tendency to depression and educational status were found to be associated with several NHP domains (P<0.001). Age and marital status showed no association with the NHP scores.
	Author's conclusions	The health related quality of life (HRQOL) of GBS patients remains lower than that of the healthy control subjects. There was a significant improvement in the functional scores in GBS patients at discharge and 6 months after rehabilitation. The reduced HRQOL after GBS appears to be related not only to the physical disability, but also to several demographic and medical variables, such as educational level, employment, gender, mechanical ventilation and psychological factors.
Meythaler 1997 [19]	Statistical analysis	Chi-square test, one-way ANOVA, Pearson's correlation coefficients.
	Results	Activity limitation <12 months - There was reduction in disability as FIM scores improved from admission to discharge: FIM motor score improved by an average of 15.7 points from mean admission score of 34.7 to mean discharge score of 50.3. The FIM cognitive score improved by an average of 6.9 points from mean admission score of 78.1 to mean discharge score of 85.
	Notes	Other outcome measures that were reported in this study included length of acute hospitalisation, length of inpatient rehabilitation, and acute and rehabilitation charges (costs). These outcome measures have not been included in this table since they were not pre-selected measures for the review.
	Author's conclusions	The requirement of prior ventilator support most strongly predicts an extended length of stay for inpatient rehabilitation and had most significant impact on total hospital length of stay (both acute and rehabilitation) and the amount of the hospital charges.
Nicholas 2000 [20]	Statistical analysis	Multiple regression analysis
	Results	Activity limitation <12 months - There was improvement in FIM and Barthel Index (BI) scores at discharge compared to admission scores: Mean modified BI score increased from 10 to 19; Mean FIM score increased from 53 to 85. Quality of life < 12 months - Environmental Status Scale (ESS) (N.=15) decreased from 23 to 13, Handicap Assessment Scale (HAS) (N.=9) decreased from 19 to 10 indicating a reduction in handicap.
	Author's conclusions	Significant improvement in function and reduction in handicap occurred during rehabilitation, which was demonstrated by standardised outcome measures.

N: total number; SD: Standard Deviation.

1) the need for high quality RCTs and CCTs, and other designs, which assess the effectiveness of specific rehabilitation interventions (components, intensity, frequency, settings). Clinical practice trials can supplement information obtained from RCTs as they can acquire prospective and retrospective data without disrupting the natural milieu of treatment. Cost effectiveness of such programmes need exploration;

2) the development of appropriate, reliable and valid outcome measures, which reflect domains of the International Classification of Functioning and Health (ICF), and a consensus on a core set of measurement of outcomes in GBS trials.[21] The ICF core sets have the potential to facilitate clinical care and agreement; incorporate the perspective of the patient (and caregiver) and may in the future assist in outcome development using ICF item banking and scale development techniques;

3) collection of longitudinal data for long term

care needs (especially psychological care) in the GBS population. These include issues related to aging with disabilities and the cumulative impact of disabilities over time in these persons.

Conclusions

The 'best' evidence to date for MDC in GBS is limited to three 'very low quality' observational studies which suggest improved disability and reduction in handicap (participation) in the short term (less than 6 months) with high intensity inpatient multidisciplinary rehabilitation. These conclusions are tentative, and the gap in current research should not be interpreted as proof that multidisciplinary care in GBS is ineffective.

References

1. Ropper AH. The Guillain-Barré Syndrome. N Engl J Med 1992;326:1130-6.
2. Hughes RA, Cornblath DR. Guillain-Barre syndrome. Lancet 2005;366:1653-66.
3. Zochodne DW. Autonomic involvement in Guillain-Barre syndrome: a review. Muscle Nerve 1994;17:1145-55.
4. Jiang GX, Chang O, Link H, de Pedro-Cuesta J. Epidemiological features of Guillain Barre syndrome in Sweden, 1976-93. J Neurol Neurosurg Psychiatry 1997;62:447-53.
5. Van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis and treatment of Guillain Barre syndrome. Lancet Neurol 2008;7:939-50.
6. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barre syndrome. J Infect Dis 1997;176(Suppl 2):S92-8.
7. Alshekhlee A, Hussain Z, Sultan B, Katirij B. Guillain Barre syndrome: incidence and mortality rates in US hospitals. Neurology 2008;70:1608-13.
8. Meythaler JM. Rehabilitation of Guillain-Barré Syndrome. Arch Phys Med Rehabil 1997;78:872-9.
9. Hughes RA, Wijdicks EF, Benson E, Cornblath DR, Hahn AF, Meythaler JM *et al.* Supportive care for patients with Guillain-Barre syndrome. Arch Neurol 2005;62:1194-8.
10. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillian-Barré syndrome. Ann Neurol 1990;27(Suppl):S21-4.
11. Hartung HP, van der Meche FG, Pollard JD. Guillain-Barre syndrome, CIDP and other chronic immune-mediated neuropathies. Curr Opin Neurol 1998;11:497-513.
12. McKhann GM. Guillain-Barre syndrome: clinical and therapeutic observations. Ann Neurol 1990;27(Suppl):S13-6.
13. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barre syndrome. Lancet Neurol 2007;6:589-94.
14. Bernsen R, de Jager AEJ, van der Meche FGA, Suurmeijer TPBM. How Guillain Barre patients experience their functioning after 1 year. Acta Neurol Scand 2005;112:51-6.
15. Forsberg A, Press R, Einarsson U, de Pedro-Cuesta J, Holmqvist LW. Disability and health related quality of life in Guillain-Barré syndrome during the first two years after onset: a prospective study. Clin Rehabil 2005;19:900.
16. Khan F, Pallant J, Ng L, Bhasker A. Factors associated with long-term functional outcomes and psychological sequelae in Guillain–Barre syndromer. J Neurol 2010; 257:2024-31.
17. The Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [updated February 2008]. In: Higgins JPT, Green S, editors. 2008.
18. Demir SO, Koseoglu F. Factors associated with health related quality of life in patients with severe Guillain Barre syndrome. Disabil Rehabil 2008;30:593–9.
19. Meythaler JM, DeVivo MJ, Braswell WC. Rehabilitation outcomes of patients who have developed Guillain-Barre syndrome. Am J Phys Med Rehabil 1997;76:411-9.
20. Nicholas R, Playford ED, Thompson AJ. A retrospective analysis of outcome in severe Guillain-Barre syndrome following combined neurological and rehabilitation management. Disabil Rehabil 2000;22:451-5.
21. World Health Organization (WHO). The International Classification of Functioning, Disability and Health (ICF). Geneva: WHO; 2001.