



Effect of Task-Oriented Approach on Functional Activity of Daily Living in Guillain Barre Syndrome

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Abstract

Background: In order for people with Guillain-Barre syndrome (GBS) to resume their independent daily lives as they did before the start of GBS, it is crucial to enhance their physical function. **Objective:** TO enhance Guillain-Barre syndrome patients' ability to carry out everyday activities, chest expansion, pain, and muscular strength. **Subjects and methods:** Twenty four adults with consistent residual impairment who were divided randomly into two equal groups six months following the beginning of GBS. In the experimental group, 60-minute sessions of task-oriented training (respiratory exercises, rocker board training, sit-to-stand training, walking five steps, up and down stairs, gait training, and foam roller massage) were assigned; in the control group, three sessions per week for a year of treatment (strengthening exercises, range-of-motion exercises, stretching exercises, and pain management) were administered. The Barthel Index was used as the primary endpoint to gauge functional independence in daily living activities, a visual analogue scale for pain intensity, muscle strength was assessed using the Medical Research Council scale, and fatigue was assessed using the Fatigue Severity Scale. **Results:** following 6 months, the median between-group difference was 3 (95% CI 2 to 4) for functional independence, while it was 7 (95% CI 7 to 7.5) for muscle strength, it was 16 (95% CI -19 to -12) for fatigue, it was 4 (95% CI 0.4 to 7) for the environment domain of quality of life, as well as it was 0.8 (95% CI 0.6 to 0.7) for chest expansion. The Estimated effects following 12 months had the same magnitude, and the majority of CIs had higher levels of uncertainty. **Conclusion:** Task oriented approach improves activity of daily living, reduced fatigue and improved strength in patient with GBS.

Keywords: Guillain Barre Syndrome, Task Oriented Approach, Activity of Daily Living.

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INTRODUCTION:

Guillain-Barre syndrome (GBS) is an uncommon but severe immune-mediated neuropathy following an infection. It is brought on by the autoimmune destruction of peripheral nervous system nerves, which causes in symptoms including numbness, tingling, and weakness that can develop into paralysis. Activity demonstrates the diagnosis and treatment of Guillain-Barre syndrome and shows how the inter-professional team can help individuals with this illness receive better care (Nguyen et al, 2019).

Since delayed therapy is linked to greater nerve damage, which delays or prevents recovery, treatment for GBS should begin as soon as the condition is diagnosed. Plasma exchange, intravenous gamma globulin therapy, and immunosuppressive medication based on immunopathology are some of the early therapies for GBS. Many GBS patients can recover to the

point where independent walking is feasible following therapy. However, even 3-6 years after the beginning of GBS, some people with the condition still have significant impacts on everyday activities and reduced muscle performance. Therefore, it is crucial for GBS patients to have rehabilitation therapy in order to boost their chances of being independent in their everyday activities and to enhance their muscle fitness (Kwang-Jun et al, 2020).

Task-oriented approach applies motor learning and motor control concepts, including rigorous training, varied practice, and intermittent feedback, in a highly personalized, client-centered rehabilitation strategy. Priority functional tasks (self-care, employment, and/or leisure activities) from task-oriented approach were heavily performed to meet functional demands such grasp-release, strengthening, and spasticity management training. The intervention identified and focused on the

crucial control parameters. Each participant's logbook was kept by the research therapists, allowing for a progressive escalation in the intervention challenge. Additionally made it possible for the therapists to assess and revise at the conclusion of each session to improve participants' compliance (Khader et al, 2016).

METHODS

Intention-to-treat analysis, the outcome assessors was blinded, and disguised allocation were all utilized in this parallel, two-group, randomized controlled trial. A 12-month task-oriented approach (experimental group) or conventional physical therapy programme were assigned to participants with persistent symptoms following GBS (control group). Between the months of October 2021 and September 2022, the study was carried out. A researcher carried out the allocation method using computer-generated block randomization with time since diagnosis stratification. Once the individual agreed to participate in the study, the sealed, opaque envelope containing each random allocation was opened to reveal the allocation sequence. Therefore, neither the researchers nor the therapists were aware of the therapy, each enrolled participant would receive. As soon as an envelope was opened, the allocated intervention was revealed to the participant as well as the therapists who administered the interventions. Results were evaluated at baseline, six and twelve months afterwards. In addition to ethical approval by research ethical committee at faculty of physical therapy, modern university for technology and information with approval number (REC/2111/MTL.PT/2211292).

SUBJECTS

The modern university for technology and information's physical treatment facility served as the study's location. Patients who had previously been diagnosed as having "definite" GBS were included in the research population. Patients with GBS had to be between the ages of 18 and 50, having a stable clinical state, and, based on assessment, having a physical handicap in order to be eligible to enroll. Pregnancy, amputation, and physical therapy in the previous six months were the exclusion criteria. Recruitment targeted those who have had the condition within six years.

INTERVENTIONS

Experimental group

The experimental group received a prescription for a 12-month, Task Oriented Approach in addition to their regular treatment from the treating physician or neurologist. Three times a week, it involved 60-minute physiotherapy sessions.

The exercises in the program involved:

* **Respiratory exercises:**

Diaphragmatic breathing exercises: the patient was taught to put one hand on upper chest while the other was positioned just below rib cage after that breathe in slowly using the nose until stomach pushed out against his hand with repetitions 3-4 times. Intercostal breathing exercises: the patients was instructed to inhale deeply and on the exhale, stretch his arms to the right, then inhale and come back to the center; on the next exhale, the patient asked to stretch his arms to the left, with repetitions 3-4 times.

* **Rocker board training**

The patient was instructed to control the rocking board's anteroposterior as well as mediolateral rolling movements by first positioning both feet, then just one, and by opening and closing their eyes alternately while sitting and standing.

* **Sit to stand**

The patient was told to lean forward, press against the heel, and then arise. When attempting to stand, place both hands on the thigh then push against it. Perform this progression ten times with your eyes open and then closed, 1st on a solid surface then on a foam surface.

* **Walk five steps forward**

The patient was instructed to take five steps forward while standing, first on a hard surface, then on a foam surface, as well as repeat this task ten times.

* **Upstairs and downstairs three steps**

The patient was instructed to take five steps upstairs, then 5 steps downstairs, with as well as without hand support.

* **Gait Training**

For ten minutes, participants walked within the parallel bar with one hand supported and then unsupported. Additionally, obstacles were used with as well as without hand support.

* **Foam roller massage**

The patient was instructed stuck the roller to the location of pain and slowly roll down the roller on the location of pain for 20-30 seconds.

Control group

Participants in the control group were given a prescription for a standard physical therapy programme lasting 60 minutes, three times per week, in addition to their regular treatment from the treating doctor or neurologist.

The program included:

* **Pain management:**

Transcutaneous Electric Nerve Stimulation [TENS] with a frequency (80– 150 Hz) was utilized. Electrodes were applied on the skin on the site of pain for thirty minutes.

*** Range of motion exercises**

Exercises were done to increase the foot's range of motion. The patient was instructed to sit in a chair, raise the involved foot, and then rotate counterclockwise and afterwards clockwise. This cycling should be repeated five and ten times in every direction.

*** Strengthening exercises:**

Strengthening of the ankle dorsiflexors, planterflexor, invertors, as well as evertors was employed as a graduate active exercise. The dorsiflexors of the ankle joint were repeatedly contracted for 10 minutes as a form of proprioceptive neuromuscular stimulation to strengthen distal muscles.

*** Stretching exercises:**

Determine shortened muscles stretch it for 10 seconds then release and repeat for three times.

OUTCOME MEASURES

Primary outcome

Based on the Barthel Index, a 10-item scale with every item scored depending on whether or not the patient is capable of finishing the task independently (scored 2), can finish the task with a little assistance (scored 1), or isn't able to finish the task (scored 0), the main outcome was functional independence in daily living activities. Greater independence is indicated by higher scores. A final score that ranges from 0 to 100 is created by adding the item scores together and multiplying the total by 5.

Secondary outcomes

*** Muscle strength:** The Manual Muscular Testing Grades were used to evaluate muscle strength. Shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, as well as foot dorsiflexors were the six muscle groups that were rated. Every muscle group received a score between 0 (no observable contraction) and 5 (normal).

*** Fatigue:** Fatigue was assessed utilizing the Fatigue Severity Scale. The participants then evaluated the overall level of their fatigue on a visual analogue scale from 0 (worst) to 10 (normal), using a range of 1 (strongly disagree) to 7 (strongly agree) to indicate how much they agreed with each of nine statements about their exhaustion.

*** Pain:** On a 100-mm visual analogue scale, where the extremes are labeled "no pain" and "unbearable pain," pain was assessed.

*** Quality of life:** Health-related quality of life was evaluated utilizing the WHOQoL-BREF, an Arabic translation of the WHO Quality of Life Scale. Each of the 26 items in this reliable and valid instrument is assessed on a 5-point scale and assesses four different domains: physical health, psychological health, social connections, as well as environmental

health. The total of a domain's item scores is the raw domain score. Then, the total score for each domain is converted to a scale from 0 to 100, with higher numbers indicating a better quality of life. Then, the total score for each domain is converted to a scale from 0 to 100, with higher numbers indicating a better quality of life (Reham et al, 2020).

*** Chest expansion measurement:** The circumference of the chest was evaluated utilizing a tape measure to determine the chest's expansion or mobility (measured in millimeters). Healthy participants' average chest expansion measurements ranged from 5.5 cm to 7.5 cm. At the xiphoid process level, the chest expanded. The patient stood during the exam while their hands were put on their heads. The purpose of the inquiry was to assess, the participants were informed. Traditionally, "breathe in maximally" and "breathe out maximally" were the instructions for measuring chest expansion. "Breathe in maximally and make yourself as big as possible" and "Breathe out maximally and make yourself as little as possible" are the instructions used to assess chest expansion. To prevent measurement mistakes and improve inter-rater reliability, the test technique was standardized, and the examiners were educated prior to the study's commencement. For each instruction, the tests were run twice, with the best result being utilized in the analysis. The difference between full expiration and inspiration, to the closest 1 mm, was the outcome of the chest expansion measurement.

DATA ANALYSIS

The statistical analysis was carried-out by utilizing statistical SPSS Package program version 25 for Windows (SPSS, Inc., Chicago, IL). Standard descriptive statistics were used to condense the baseline data. The Kolmogorov Smirnov test was utilized to find that the outcome measures' data distribution did not follow a normal distribution, and non-parametric statistics were utilized for the following studies. To quantify the impact of the experimental intervention in comparison to the control intervention, outcomes were compared between groups. Using the Campbell and Gardner approach, the median difference for each of these estimations was determined along with a 95% confidence interval.

This methodology designated a sample size that was determined using free software. Calculations of the expected standard deviation of the Barthel Index in GBS were not considered to be reliable since we did not know what the smallest worthwhile impact in GBS would be and since the estimate could only be determined from a relatively small cohort study that had various eligibility criteria. Since the CIs would show the accuracy with which the study's ultimate estimates of

therapy's effects may be made, they are an essential part of any efficacy study; we decided to enroll as many patients as we could within the constraints of the study's resources.

RESULTS

Adherence to the trial's guidelines

As stated in the registered protocol, the interventions were used. No unregistered outcomes

were reported; all primary and secondary outcomes that were registered were reported.

Participants' progression through the study

24 individuals were randomly assigned evenly to each group (12 patients per group) after 37 patients had been screened. Each participant completed the research in its entirety and submitted information on each outcome measure at each appointment time. The movement of patients through the research is depicted in **Figure 1**.

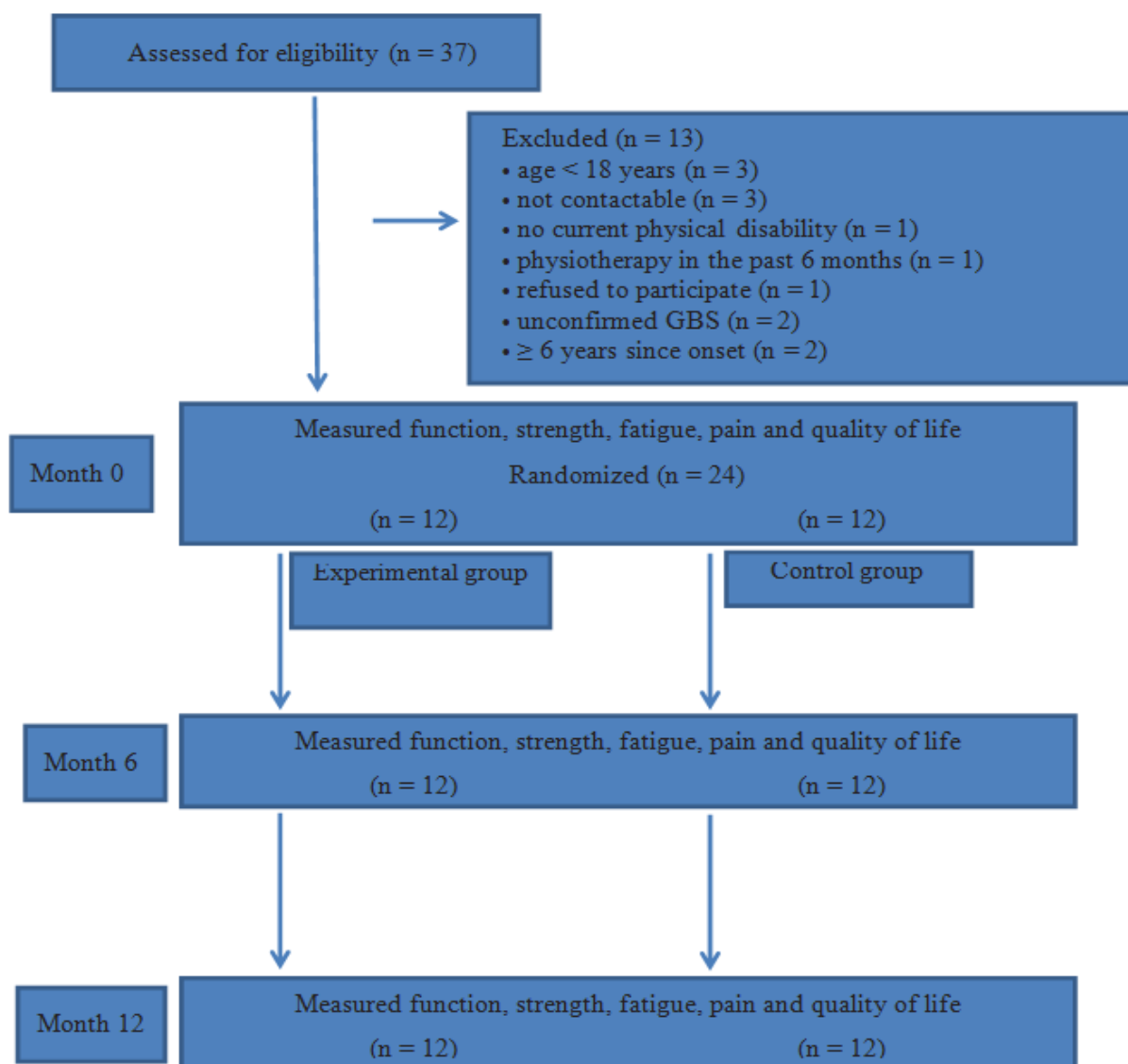


Figure 1. Flowchart.

Participant characteristics in the study

Both the pre-treatment scores on the outcome measures and the demographic features of the two

groups (Table 1) were comparable (first two columns of data in Tables 2 and 3).

Table 1. The research participants' characteristics.

Characteristic	Exp (n = 12)	Con (n = 12)
Age (yr), mean (SD)	30 (2.01)	45 (3.39)
Gender, n (%)		
female	5 (41.7)	5 (41.7)
male	7 (58.3)	7 (58.3)
Education (yr), mean (SD)	11.8 (0.70)	11.7 (1.10)
Married, n (%)	7 (58.3)	9 (75)
Fatigue	1 (8.3)	2 (16.7)
Paraparesis/difficulty walking	2 (16.7)	3 (25)
Pain	1 (8.3)	3 (25)
Hand weakness	1 (8.3)	3 (25)
Facial weakness	2 (16.7)	1 (8.3)

Due to the effects of rounding, certain percentages do not add up to 100. Con = control group, Exp = experimental.

OUTCOMES OF THE INTERVENTION

Primary outcome

In all groups, functional independence increased, in favor of the experimental group (Table 2). The median difference in improvement in the 100-point Barthel Index between groups at month six was 3 points (95% CI: 2 to 4). The experimental intervention might not enhance the Barthel Index greater than the control intervention, but it is unlikely to be less beneficial, according to the lower limit of the CI. The top limit suggested that the experimental intervention may outperform the control intervention significantly. Following 12 months, the outcome changed (median difference of 5 points, 95% confidence interval: 6 to 10).

Secondary outcomes

Strengthening of muscles: In both groups, but especially in the experimental group, muscle strength increased (Table 2). On the 60-point Medical Research Council measure, the median between-group difference in improvement at month 6 was 7 points (95% CI: 7 to 7.5). The CI showed that there is some ambiguity regarding the precise advantage, but it also demonstrated that the improvement of muscle strength was greater in experimental intervention than the control intervention. The outcome at month 12 was relatively comparable (median difference of 10 points, 95% confidence interval: 8 to 10).

Fatigue: Both groups had less fatigue, but the experimental group experienced it more (Table 2). The median difference in improvement on the 63-point Fatigue Severity Scale across groups at month six was 16 points (95% CI 12 to 19). The CI showed considerable ambiguity regarding the precise effect, ranging from a potentially insignificant benefit (i.e., a decline of 1 point on the Fatigue Severity Scale) to a significant

advantage (i.e., a 19-point reduction). It did, however, demonstrate that the experimental intervention lessens tiredness greater than the control intervention. The CI revealed considerably higher uncertainty, including the likelihood that there would be no larger benefit than the control intervention, despite the fact that the primary estimate following 12 months was significantly more useful (median difference 18 points).

Pain: Average pain intensity seemed to decrease in the experimental group, whereas the control group showed no discernible improvement (Table 2). The experimental group's pain intensity was estimated to have decreased by 0.6 points greater than the control group's following 6 months (95% CI: 0.2 to 1.2). Pain may be significantly reduced by the experimental intervention compared to the control intervention (i.e., by 1.2 points on a 0-to-10 VAS), or it might not decrease pain greater than the control intervention, however it is unlikely to increase pain, according to the limits of the CI. At month 12, the impact was less certain.

Quality of life: The WHOQoL-environment BREF's domain showed the most obvious improvement in quality of life (Table 3). It demonstrated a distinct but modest benefit at month 6 (median difference of 4 points, 95% CI 0.4 to 7). Despite the fact that the median difference at month 12 was considerably larger, this estimate had much wider uncertainty; the CI ranged from no effect to a significant effect (i.e., 10 points on the 100-point scale). In months 6 and 12, as well as at month 12, the psychological and physical health domains both produced estimates that were equally encouraging yet ambiguous. Despite having large CIs, all other key estimations favored the experimental group.

Chest Expansion: Both groups experienced increases in chest expansion, whereas the experimental group experienced a greater increase (Table 2). There was a 0.8-point (95% CI 0.6-0.7) median improvement between the two groups following 6 months. There was little to no difference in the outcome following 12 months (median difference 1.6 points, 95% CI 1.5 to 1.7).

Table 2. The median results for each group, the median between-group difference, and the median within-group difference (95% CI) for symptom scores.

Variable	Between-group difference					
	Baseline		Month 6		Month 12	
	Exp	Con	Exp	Con	Exp	Con
	(n = 12)	(n = 12)	(n = 12)	(n = 12)	(n = 12)	(n = 12)
Barthel Index (0 to 100)	89 (86 to 92)	90 (89 to 91)	94 (91 to 97)	91 (90 to 92)	99 (98 to 100)	95 (94 to 96)
MRC scale (0 to 60)	37 (35 to 38)	40 (39 to 41)	45 (41 to 46)	47 (46 to 48)	49 (46 to 51)	47 (46 to 49)
Fatigue Severity Scale (0 to 63)	53 (50 to 54)	53 (48 to 54)	29 (27 to 30)	45 (41 to 46)	19 (18 to 20)	49 (45 to 50)
Pain VAS (0 to 10)	7 (6 to 8)	7 (6 to 8)	5 (4 to 7)	7 (7 to 8)	2 (2 to 3)	8 (7 to 9)
Chest expansion	1.7 (1.6 to 1.8)	1.6 (1.5 to 1.7)	3 (2.9 to 3.1)	2.1 (2 to 2.2)	4.2 (4.1 to 4.3)	2.5 (2.4 to 2.6)
Variable	Within-group difference					
	Month 6 minus baseline		Month 12 minus baseline		Month 6 minus baseline	Month 12 minus baseline
	Exp	Con	Exp	Con	Exp minus Con	Exp minus Con
	(n = 12)	(n = 12)	(n = 12)	(n = 12)		
Barthel Index (0 to 100)	5 (5 to 6)	0.9 (0.8 to 0.9)	11 (10 to 12)	4.5 (4.5 to 5)	3 (2 to 4)	5 (6 to 10)
MRC scale (0 to 60)	7 (6 to 7)	8 (7 to 8)	12 (11 to 12)	7.5 (7 to 8)	7 (7 to 7.5)	10 (8 to 10)
Fatigue Severity Scale (0 to 63)	-24 (-24 to -22)	-8 (-8 to -7)	-34 (-35 to -32)	-4 (-4 to -3.7)	-16 (-19 to -12)	-18 (-12 to -25)
Pain VAS (0 to 10)	-2 (-2.5 to -2)	0.5 (0.4 to 0.5)	-5 (-5 to -4)	1 (0.9 to 1)	-0.6 (-0.2 to -1.2)	-1.5 (-3 to -0.6)
Chest expansion	1.3 (1.2 to 1.4)	0.5 (0.4 to 0.6)	2.5 (2.4 to 2.5)	0.9 (.8 to 1)	0.8 (0.6 to 0.7)	1.6 (1.5 to 1.7)

Con = control group, Exp = experimental group, MRC = Medical Research Council, VAS = visual analogue scale.

Table 3. For quality-of-life domains, the median (IQR) results for each group, the median (IQR) between-group difference, and the median (IQR) within-group difference are shown.

Variable	Between-group difference					
	Baseline		Month 6		Month 12	
	Exp	Con	Exp	Con	Exp	Con
	(n = 12)	(n = 12)	(n = 12)	(n = 12)	(n = 12)	(n = 12)
Physical health	43 (40 to 44)	44 (43 to 46)	61 (57 to 62)	45 (44 to 47)	67 (62 to 69)	46 (45 to 48)
Psychological	51 (48 to 52)	51 (49 to 53)	67 (64 to 69)	59 (56 to 59)	71 (68 to 73)	61 (58 to 62)
Social relationships	35 (33 to 38)	36 (34 to 39)	69 (64 to 75)	61 (57 to 66)	67 (63 to 74)	60 (56 to 65)
Environment	45 (42 to 49)	47 (44 to 48)	55 (52 to 60)	43 (41 to 44)	59 (55 to 65)	43 (41 to 44)
Variable	Within-group difference					
	Month 6 minus baseline		Month 12 minus baseline		Month 6 minus baseline	Month 12 minus baseline
	Exp	Con	Exp	Con	Exp minus Con	Exp minus Con
	(n = 12)	(n = 12)	(n = 12)	(n = 12)		
Physical health	18 (17 to 19)	1 (0.9 to 1)	24 (22 to 25)	2 (2 to 2)	8 (6 to 13)	11 (8 to 18)
Psychological	16 (15 to 17)	7 (6.7 to 7)	71 (68 to 73)	9 (8.6 to 9)	11 (10 to 14)	36 (26 to 53)
Social relationships	34 (32 to 37)	25 (23 to 27)	33 (30 to 36)	24 (22 to 26)	29 (27 to 32)	27 (26 to 28)
Environment	11 (10 to 12)	-4 (-4 to -3)	15 (13 to 16)	-3.5 (-4 to -3)	4 (0.4 to 7)	5.5 (2 to 10)

Con = control group, Exp = experimental group, WHOQoL-BREF = World Health Organization Quality of Life questionnaire.

DISCUSSION:

The main results of this experiment show that gaining functional independence with daily living tasks may be accomplished with a task-oriented approach programme with pain management on par with or better than a conventional physical therapy programme. Muscular strength, tiredness, and one quality of life dimension were the secondary end measures that revealed more definite estimates of benefit following 6 months, with the beneficial impact on muscle strength still being obviously discernible following 12 months.

The study had several characteristics that lend credence to the results: it came in agreement with the prospectively registered protocol; Investigators were blinded to treatment group for the main outcome as well as the objective secondary outcomes; all patients were monitored for a full year; allocation was really randomized with concealment of the allocation list throughout recruitment; The data was analyzed using the intent-to-treat method, providing confidence intervals (CIs) to demonstrate the reliability of the findings. GBS is an uncommon condition that affects one to two persons per 100,000 people.

For enhancing functional independence with activities of daily living, the task-oriented approach programme is either better than or as good as the conventional physical therapy programme, according to estimations from the primary outcome measure with 95% confidence intervals. GBS can seriously impair one's capacity for doing daily tasks. Despite the uncertainty surrounding the average impact on independence, patients who are extremely dissatisfied by this may decide that it is worthwhile to attempt the task-oriented approach programme, especially considering the effects on other outcomes, which were more definite. Any conclusion regarding the importance of the supervised programme should take into account all of the effects that were recognized rather than just determining whether a particular benefit is worthy. Excessive travelling to exercise sessions may be the main drawback of the task oriented approach training if the effort and risk required in doing the exercise are comparable in both settings (**Simatos et al, 2016**).

Among the most obvious advantages was an improvement in muscle strength that was maintained effectively from month 6 through month 12. Since **Lhassan et al. (2017)** detected in their prospective cohort research that strength rose considerably within the first 6 months ($P < 0.01$), they proposed a task-oriented approach programme. Muscle strength grew less quickly between 6 and 18 months ($P < 0.05$). We found a significant negative connection ($\rho = -0.82$; $P = 0.05$) between the length of the plateau period and the recovery of knee extensor and elbow flexor muscle strength. Manual muscle testing results and functional independence motor total scores were

about normal at 6 months. All patients met the requirements for a complete recovery at 18 months. Fatigue is one of the symptoms of GBS that is regarded as being the most incapacitating. The current study's CI for the between-group comparison of tiredness following month 6 varied from a marginal benefit to a potentially valuable advantage. The benefit on tiredness in the current research is credible as task-oriented training has been shown to reduce fatigue in GBS patients (**Ranjani et al, 2014**).

Prevalence is 66% during the acute phase and 33% one year after the onset of symptoms, pain is observed in all periods of GBS. The absence of a pain decrease in the control group may have been because the present individuals had already passed the acute phase. At six months, the task-oriented training programme may or may not decrease pain greater than the control intervention (i.e., a decrease on the 0-to-10 visual analogue scale), but it is unlikely to generate any additional discomfort. In general, exercises are successful in treating chronic musculoskeletal discomfort (**Babatunde et al, 2017**).

Anxiety, sadness, and a decline in quality of life are typical long-term deleterious effects of GBS. At month 6, environmental quality of life showed the greatest improvement from the supervised programme, in contrast to the other research. This suggests improved replies to inquiries on the availability of leisure activities, the accessibility of transportation alternatives, the availability of healthcare facilities, and feelings of safety. Patients may be able to accomplish these crucial parts of life with increased strength and reduced weariness (**Hillyar and Nibber, 2020**).

Patients with Guillain-Barre syndrome who have been followed for a significant amount of time have showed residual impairment in terms of motor and sensory function, as well as in terms of the incidence of pain, exhaustion, a reduction in quality of life, and general functioning. Long-lasting functional impairment has been demonstrated to be related with acute respiratory impairment. However, studies have shown that breathing exercises to increase chest expansion can gradually restore lung function values, leading to practically full recovery and no apparent residual damage after two years of illness (**Merkies and Kieseier, 2016**).

According to the primary outcome of the study by **Nehal et al. (2022)**, a physiotherapist-supervised, individualized exercise program combined with pain treatment is as effective as or more effective than standard care in enhancing functional independence with ADLs. Muscle strength, fatigue, and one aspect of quality of life were found as secondary outcomes with more confident estimates of improvement at 6 months, with the positive impact on muscle strength persisting clearly after 12 months.

CONCLUSION:

Task oriented approach improves activity of daily living, reduced fatigue and improved strength in patient with GBS.

AUTHORS' CONTRIBUTIONS

Authors were responsible for the conceptualization of the study, data collection, statistical analysis, and preparation of the first draft of the article and editing of the article.

Conflicts of Interest

The authors have declared that no competing interests exist.

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Most research funding comes from one source, corporations of authors

Data Availability

The data used to support the findings this study are available from the corresponding author upon request.

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