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ORIGINAL RESEARCH

Efficacy of Tacrolimus Plus Prednisone as Long-Term Immunosuppressive Therapy for Chronic Inflammatory Demyelinating Polyneuropathy: A Retrospective Cohort Study

Li Di, Xinmei Wen, Wenjia Zhu, Min Wang, Yan Lu, Min Xu, Hai Chen, Yuwei Da

Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, People's Republic of China

Correspondence: Yuwei Da, Department of Neurology, Xuanwu Hospital, Capital Medical University, 45 Changchun Street, Xicheng, Beijing, 100053, People's Republic of China, Email dayuwei100@hotmail.com

Purpose: This study aimed to evaluate the efficacy and safety of tacrolimus as an add-on therapy in patients with chronic inflammatory demyelinating polyneuropathy (CIDP).

Patients and Methods: This retrospective cohort analysis was conducted using data from CIDP patients in the database of Xuanwu Hospital, Capital Medical University between April 2019 and June 2023. This study compared the efficacy of tacrolimus plus prednisone (T&P) versus prednisone monotherapy (PM) as maintenance immunosuppressive therapy. The primary endpoint was the response rate, defined as ≥1-point improvement in INCAT score, assessed at 3, 6, and 12 months. Secondary endpoints included: (1) I-RODS score changes from baseline to 3, 6, and 12 months; (2) the monthly median daily prednisone dose; (3) relapse rate (INCAT score worsening ≥1 point) in the 12-month follow-up; and (4) adverse event profiles over the 12-month follow-up period.

Results: Among 74 screened CIDP patients, 34 (45.9%) were included, with 16 receiving T&P and 18 receiving PM. All patients completed follow-up (median: 1.4 years; range: 1.0–6.5 years). The T&P group demonstrated significantly higher response rates at 3 and 6 months compared to PM, though this difference attenuated by 12 months. I-RODS improvements were significantly greater in the T&P group at all time points. The relapse rate was lower in the T&P group (12.5% vs 33.3%). The T&P group maintained significantly lower prednisone doses from month 2 onward, with higher prednisone discontinuation rates at 12 months (43.8% vs 11.1%; p=0.01). Both groups showed comparable safety profiles, with no serious adverse reactions reported.

Conclusion: Tacrolimus plus prednisone therapy demonstrated superior clinical outcomes compared to prednisone monotherapy in CIDP maintenance treatment, including accelerated symptomatic improvement, reduced relapse risk, and facilitated corticosteroid tapering. The combination regimen maintained an acceptable safety profile without serious adverse events, supporting its corticosteroid-sparing role in CIDP management.

Keywords: chronic inflammatory demyelinating polyneuropathy, CIDP, tacrolimus, prednisone, immunosuppressive therapy

Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is the most common chronic autoimmune peripheral nervous system disorder.[1] Its immunopathogenesis involves synergistic immune-mediated damage to peripheral nerve myelin, involving cell-mediated, humoral, and cytokine-driven pathways.[2] Central to CIDP immunopathology is the activation of T lymphocytes: naïve T cells are primed by antigen-presenting cells, undergo clonal expansion and differentiation into effector T cells, and migrate across the blood-nerve barrier via chemokine signaling and adhesion molecule interactions. These activated T cells drive inflammatory responses, recruit macrophages, and promote sustained demyelination.[3] Nerve histopathology has confirmed endoneurial infiltrates of CD4+, CD8+ T cells and macrophage-mediated demyelination.[4] This immune cascade provides a compelling rationale for targeting T-cell activation in CIDP management. Although no definitive antibody has been identified in typical CIDP. The efficacy of plasma exchange and

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efgartigimod—a neonatal Fc receptor (FcRn) blocker[5]—which remove circulating IgG and other humoral factors, supports the involvement of a humoral-mediated immunopathological mechanism.

Current treatment guidelines recommend intravenous immunoglobulin (IVIg), corticosteroids, and plasma exchange as first-line therapies for CIDP.[6] However, the widespread use of IVIg is limited by its high cost and restricted availability. Plasma exchange is often impractical in many clinical settings due to its dependence on specialized equipment, the requirement for central venous access, and the need for inpatient care. In contrast, corticosteroid therapy remains the most convenient and cost-effective option for CIDP. Nevertheless, it is consistently associated with dose-dependent adverse effects, such as hyperglycemia, osteoporosis, obesity, and cardiovascular complications. Strategies aimed at reducing cumulative steroid exposure, while minimizing relapse risk are highly desirable, as they could yield multifaceted benefits. Firstly, reducing the cumulative steroid dose would directly mitigate the risk and severity of adverse events, thereby decreasing the need for concomitant medications and associated costs. More importantly, effective steroid-sparing strategies can help sustain remission and reduce relapse frequency, which not only improves long-term outcomes but also alleviates the economic burden of relapse management, including the costs of rescue therapies such as IVIg or rehospitalization. In response to these challenges, the 2021 European Academy of Neurology–Peripheral Nerve Society (EAN/PNS) guidelines for CIDP proposed incorporating immunosuppressant or immunomodulatory drugs as steroid-sparing agents.[6] Although agents such as azathioprine, mycophenolate mofetil, and cyclosporine are recommended, the supporting evidence remains of very low certainty.[7–9]

Tacrolimus, a calcineurin inhibitor, selectively suppresses T-lymphocyte proliferation and interleukin-2 (IL-2) transcription.[10] Initially developed for organ transplantation, it is now widely used in the treatment of various immune-mediated diseases, including systemic lupus erythematosus,[11,12] minimal change nephrotic syndrome,[13,14] myositis-associated interstitial lung disease,[15] and myasthenia gravis.[16,17] Emerging evidence suggests potential benefits of tacrolimus in in the management of CIDP.[18–20] However, the 2021 EAN/PNS CIDP guidelines recommend against its use owing to limited efficacy data and concerns over potential adverse effects,[6] particularly tacrolimus-induced peripheral neuropathy which has been reported in organ transplant recipients. The pathophysiological mechanisms underlying this neurotoxic effect remain poorly understood.

Given the well-established inhibitory effect of tacrolimus on T-cell function,[21] the central role of T-cell activation in the immunopathogenesis of CIDP,[3] and the encouraging therapeutic outcomes observed in previous case series,[18–20] this retrospective cohort study was designed to systematically evaluate the efficacy and safety of tacrolimus plus prednisone as long-term immunosuppressive therapy for CIDP, with specific emphasis on relapse prevention and corticosteroid-sparing effects.

Materials and Methods

Study Design and Participants

This was a retrospective cohort study conducted at a single tertiary hospital, approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University (No. 2023-235-003). Written informed consent was obtained from all participants for inclusion in the Xuanwu Hospital CIDP database and for the use of their data in subsequent research.

All consecutive patients in the CIDP database of Xuanwu Hospital from April 2019 to June 2023 were analyzed. Inclusion criteria were as follows: 1) Patients (male or female) aged ≥ 18 years; 2) Diagnosis of CIDP according to the 2021 EAN/PNS guidelines;[6] 3) Baseline inflammatory neuropathy cause and treatment score (INCAT) disability score ≥ 2; 4) Receiving either prednisone monotherapy (PM) or tacrolimus plus prednisone (T&P) therapy as maintenance treatment, with ≥12 months of follow-up. Exclusion criteria included: 1) CIDP associated with monoclonal gammopathy of unknown significance (MGUS); 2) Autoimmune nodopathies, are characterized by the presence of autoantibodies targeting nodal and paranodal proteins—such as neurofascin-155 (NF155), contactin-1 (CNTN1), contactin-associated protein 1 (Caspr1) or neurofascin isoforms NF140/186; 3) Incomplete follow-up clinical data; 4) Use of other non-steroidal immunosuppressants or monoclonal antibody therapies as maintenance treatment.

Therapeutic Regimen and Follow-up

Upon confirmation of the CIDP diagnosis, the initial therapeutic intervention consisted of either IVIg or pulsed intravenous methylprednisolone. The treatment modality was selected through shared decision-making between treating physicians and patients. IVIg was administered at 2 g/kg divided over 5 consecutive days. Pulsed IV methylprednisolone was given at 500 mg/day for 3 days. Subsequently, the patient chose either oral prednisone monotherapy (PM) or tacrolimus plus prednisone (T&P) therapy as maintenance immunotherapy. Oral prednisone was initiated at 10 to 60 mg daily, adjusted according to clinical response to initial therapy. Tacrolimus was started at 2 mg/day, with dose adjustments guided by trough concentrations (target: 5–10 ng/mL) and toxicity monitoring. Prednisone was tapered to the minimal effective dose, with titration regimens individualized based on therapeutic response and tolerance at monthly follow-ups (Figure 1).

Relapse, defined as ≥1-point INCAT score worsening, was managed with: 1) Oral prednisone (max 1 mg/kg/day), 2) IV methylprednisolone pulses (500 mg/day ×3 days), or 3) IVIg (2 g/kg over 5 days) – selected by clinical assessment, prior response, and patient preference.

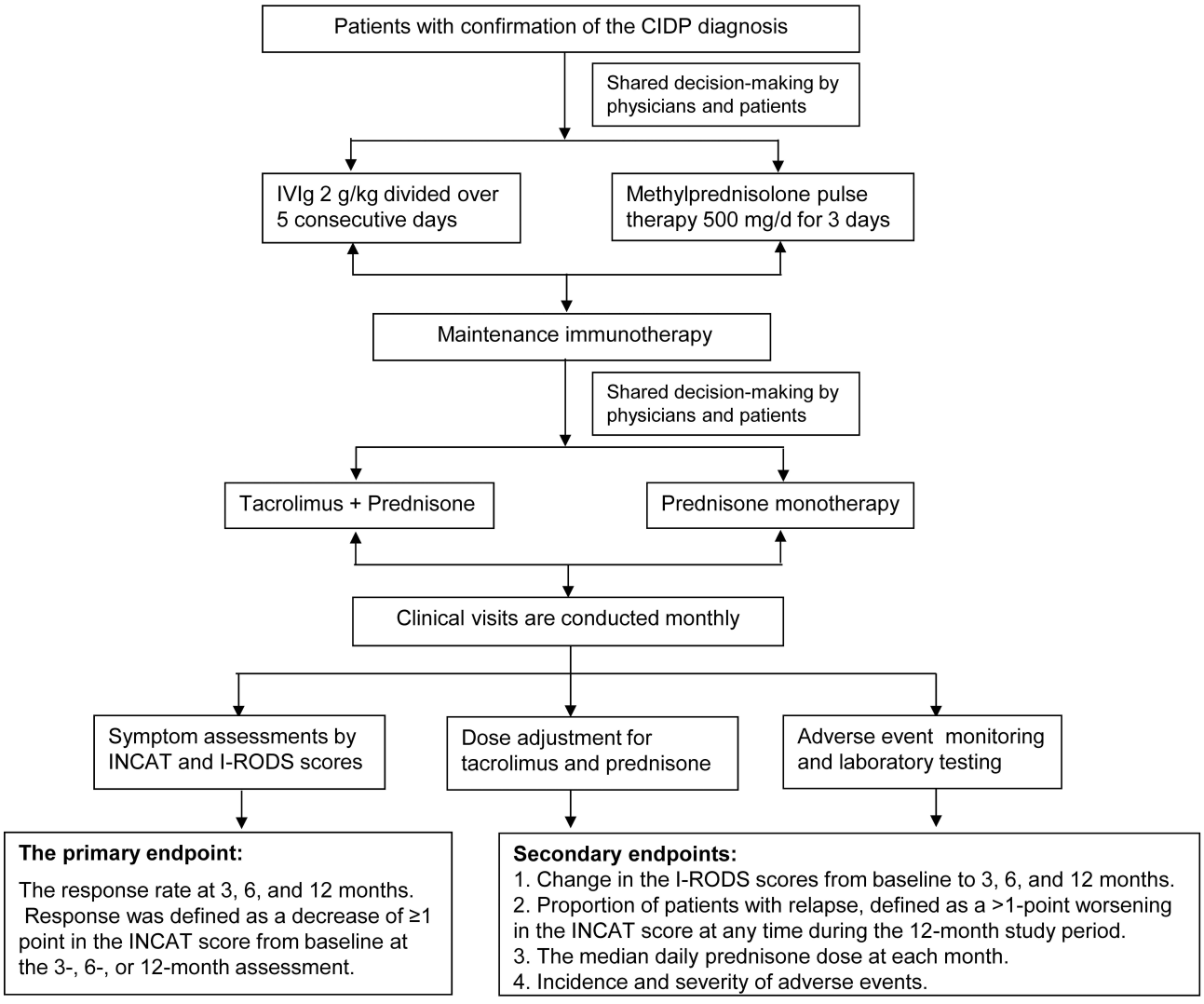

Figure 1 Schematic of the assigned therapeutic regimens, scheduled follow-up assessments, and primary/secondary outcome measures utilized for clinical evaluation.
Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; IVIg, intravenous Immunoglobulin; IV, intravenous; INCAT, Inflammatory Neuropathy Cause and Treatment Disability; I-RODS, Inflammatory Rasch-built Overall Disability Scale.

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Follow-up protocol: monthly clinic visits for symptom assessment (using INCAT and I-RODS), dose adjustment, and adverse event (AE) monitoring (per standard reporting criteria). Tests included: complete blood count (CBC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), creatinine, blood urea nitrogen (BUN), random glucose, and tacrolimus trough levels, every 2 weeks for the first 8 weeks, monthly thereafter.

Outcomes Measures

The primary endpoint was the response rates at 3 months, 6 months and 12 months. A Response was defined as a decrease of ≥1 point in the INCAT disability score from baseline to 3 months, 6 months and 12 months. Secondary endpoints included changes in I-RODS scores from baseline to 3 months, 6 months, and 12 months; the relapse rate (defined as >1-point worsening in INCAT score) over 12 months; and the median daily prednisone dose per month (Figure 1). Safety assessment included the incidence of treatment-emergent adverse events (TEAEs), discontinuations due to TEAEs, and serious TEAEs. Adverse events graded per the National Cancer Institute's Common Terminology Criteria for Adverse Events version 5.0. Whether adverse events were treatment related or not was judged by the treating physicians. To assess causality, each AE was systematically evaluated using the World Health Organization-Uppsala Monitoring Centre Causality Assessment (WHO-UMC) criteria. This tool categorizes the likelihood of causation as Certain, Probable, Possible, Unlikely, Unclassified, Unassessable. Only AEs rated as "Possible" or above were considered treatment-related for the analysis in this study.

Data Collection

The following data were collected: 1) demographic data; 2) diagnostic data, including clinical and electrophysiological findings for CIDP diagnosis and CIDP subtype. These data were individually evaluated by one of the investigators with the most clinical diagnostic experience to ensure diagnostic homogeneity; 3) disease duration from onset to the time of treatment initiation at our center, and the presence of comorbidities with functional impact; 4) data on initial treatments and the drug doses used in maintenance treatment at each follow-up; 5) data on treatment response and 6) All adverse events (AEs) were recorded and graded for severity.

Statistical Analysis

Descriptive statistics, including mean and standard deviation (SD), percentages, medians, and interquartile ranges, were used to describe demographic and clinical characteristics. Student's t test or Mann–Whitney U-test was used for quantitative variables, while the chi-square test or Fisher's exact test was used for categorical variables when appropriate. Missing data were handled using the last observation carried forward method. All statistical analyses were performed using SPSS version 25.0 and GraphPad Prism version 8.4. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Results

Demographic Characteristics of the Subjects

Between April 2019 and June 2023, a total of 74 cases were included in the CIDP database of Xuanwu Hospital, Capital Medical University. Forty cases were excluded from the present study for the following reasons: autoimmune nodopathies (n=27), MGUS comorbidity (n=4), incomplete follow-up documentation (n=4), and baseline INCAT scores ≤1 (n=5). The final cohort comprised 34 CIDP patients who completed at least 12 months of follow-up, including 25 males and 9 females (male-to-female ratio: 2.8:1) (Figure 2).

Table 1 summarizes the demographic and clinical characteristics of the 34 CIDP patients included in this study. The cohort had a mean age of 48 years (range: 16–75) and a median disease duration of 12 (6,18) months. Based on clinical phenotypes, the majority of patients presented with typical CIDP (n=24, 70.6%), followed by multifocal CIDP (n=6, 17.6%) and motor-predominant CIDP (n=4, 11.8%). Regarding disease course patterns, a relapsing-remitting course was observed in 20 patients (58.8%), while 14 patients (41.2%) exhibited a chronic progressive course.

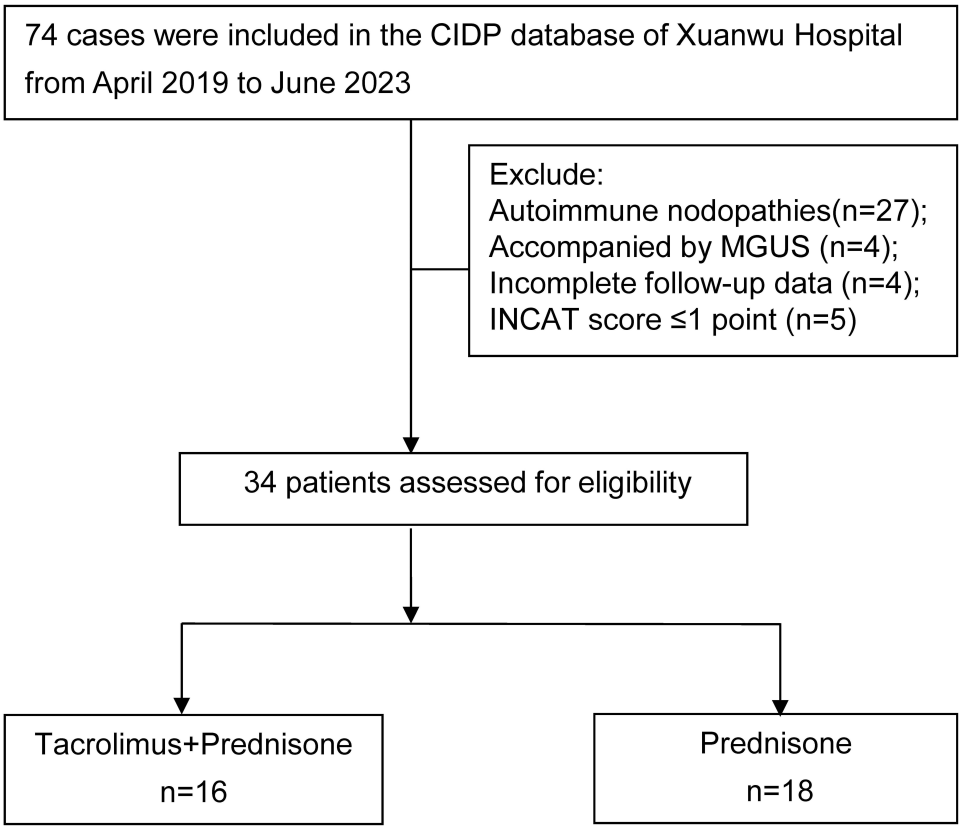

Figure 2 A flow chart for subject selection and clinical characteristics of patients.
Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; MGUS, monoclonal gammopathy of unknown significance; INCAT, Inflammatory Neuropathy Cause and Treatment Disability; TAC, tacrolimus.

The induction therapy regimen consisted of intravenous methylprednisolone pulse therapy in 23 patients (67.6%) and IVIg in 11 patients (32.4%). At baseline, the mean INCAT disability score was 4.4 ± 1.5, and the mean I-RODS score was 24.9 ± 14.8. For maintenance therapy, 18 patients received prednisone monotherapy (PM), while 16 patients were treated with the tacrolimus plus prednisone (T&P) therapy. Comparative analysis revealed no significant differences between the two maintenance therapy groups regarding demographic characteristics (age, gender), clinical features (disease duration, CIDP subtypes), or baseline functional scores (INCAT and I-RODS). Furthermore, the distribution of initial induction therapies (intravenous methylprednisolone vs IVIg) showed no significant intergroup difference. The median follow-up duration for the entire cohort was 1.4 years (range: 1.0–6.5 years).

Treatment Efficacy

At the 3-month follow-up, a significantly higher proportion of patients in the T&P group achieved clinically meaningful improvement (≥1-point reduction in INCAT score) compared to the PM group (62.5% vs 44.4%, $p = 0.02$). This treatment effect persisted at 6 months, with 81.3% of T&P-treated patients showing improvement versus 55.6% in the PM group ($p = 0.01$). By 12-month follow-up, while the T&P group maintained an 81.3% response rate, the PM group showed increased improvement to 72.2%, resulting in a nonsignificant between-group difference ($p = 0.10$).

Both treatment groups demonstrated significant I-RODS score improvements at all time points, with the T&P group showing superior outcomes. From baseline to 3 months, the T&P group had a mean I-RODS improvement of 15.4 ± 10.8 points, significantly greater than the PM group's 10.4±12.1-point improvement ($p = 0.01$). This advantage persisted at 6 months (18.8±8.4 in the T&P group versus 14.7±10.1 in the PM group, $p=0.02$) and remained significant at 12 months (19.0 ±9.4 vs 16.1±12.1; $p=0.02$). The T&P group showed a significantly lower relapse rate compared to the PM group (12.5% [2/16] vs 33.3% [6/18]; $p=0.01$) over the 12-month follow-up period (Table 2).

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Table 1 Demographics and Clinical Characteristics of Patients at Baseline

	Overall N =34	T&P Group N=16	PM Group N=18	*P* value
Age (years)				
Mean ± SD	48 ± 15.6	46 ± 15.8	49 ± 15.1	0.25
Min-max	18–75	18–65	25–75	
Gender, N (%)				
Male	25 (73.5%)	12 (75.0%)	13(72.2%)	0.65
Female	9 (26.5%)	4 (25.0%)	5(27.8%)	0.55
Disease duration (months)				
Median (IQR)	12 (6,18)	12 (8,18)	18 (6,18)	0.066
Min-max	2–229	2–229	6–67	
Categories of CIDP, N (%)				
Typical	24 (70.6%)	11(68.7%)	13(72.2%)	0.22
Multifocal	6 (17.6%)	3(18.8%)	3(16.7%)	0.79
Motor-predominant	4 (11.8%)	2(12.5%)	2(11.1%)	0.33
Relapsing-remitting type	20(58.8%)	10(62.5%)	10(55.6%)	0.56
Chronic progressive type	14(41.2%)	6(37.5%)	8(44.4%)	0.41
Initial treatment, N (%)				
IVIg	11(32.4%)	5 (31.3%)	6 (33.3%)	0.55
Methylprednisolone pulse	23(67.6%)	11 (68.7%)	12 (66.7%)	0.45
INCAT score				
Mean ± SD	4.4±1.5	4. 5±1.8	4.3±1.3	0.48
Min-max	2–8	2–8	2–8	
I-RODS				
Mean ± SD	24.9±14.8	24.2±13.8	25.8±15.1	0.44
Min-max	4–42	4–42	4–42	

Note: *P*< 0.05 was statistical difference.
Abbreviations: T&P, tacrolimus plus prednisone; PM, prednisone monotherapy.

Table 2 Comparison of Outcome Measures Between Tacrolimus Plus Prednisone Therapy and Prednisone Monotherapy at Different Follow-up Time Points

	Overall N =34	T&P Group N=16	PM Group N=18	*P* value
Number of responders N (%)[a]				
3 months	18(52.9%)	10(62.5%)	8(44.4%)	**0.02**
6 months	23(67.6%)	13(81.3%)	10(55.6%)	**0.01**
12 months	26(76.5%)	13(81.3%)	13(72.2%)	0.10
Change of I-RODS				
3 months	12.1±11.4	15.4±10.8	10.4±12.1	**0.01**
6 months	17.2± 9.5	18.8±8.4	14.7±10.1	**0.02**
12 months	17.9±10.4	19.0±9.4	16.1±12.1	**0.02**
Relapse in 12 months N (%)	8(23.5%)	2(12.5%)	6(33.3%)	**0.01**
Prednisone discontinuation N (%)	9(26.5%)	7(43.8%)	2(11.1%)	**0.001**

Notes: [a]Responders were defined as ≥1-point improvement in the INCAT disability score. *P*< 0.05 was statistical difference. *P*-values in bold indicate statistically significant differences between the two groups.
Abbreviations: T&P, tacrolimus plus prednisone; PM, prednisone monotherapy.

From month 2 onward, the T&P group maintained significantly lower median daily prednisone doses than the PM group (Figure 3). Both groups showed dose escalations at 9 months (PM group) and 10 months (T&P group), coinciding with relapse. Notably, the median daily prednisone dose before relapse was lower in the T&P group (7.0±3.5 mg) than in the PM group (20.2±12.5 mg). At 12 months, the T&P group's median dose was 3.3±3.0 mg versus 10.5±7.5 mg in the PM group

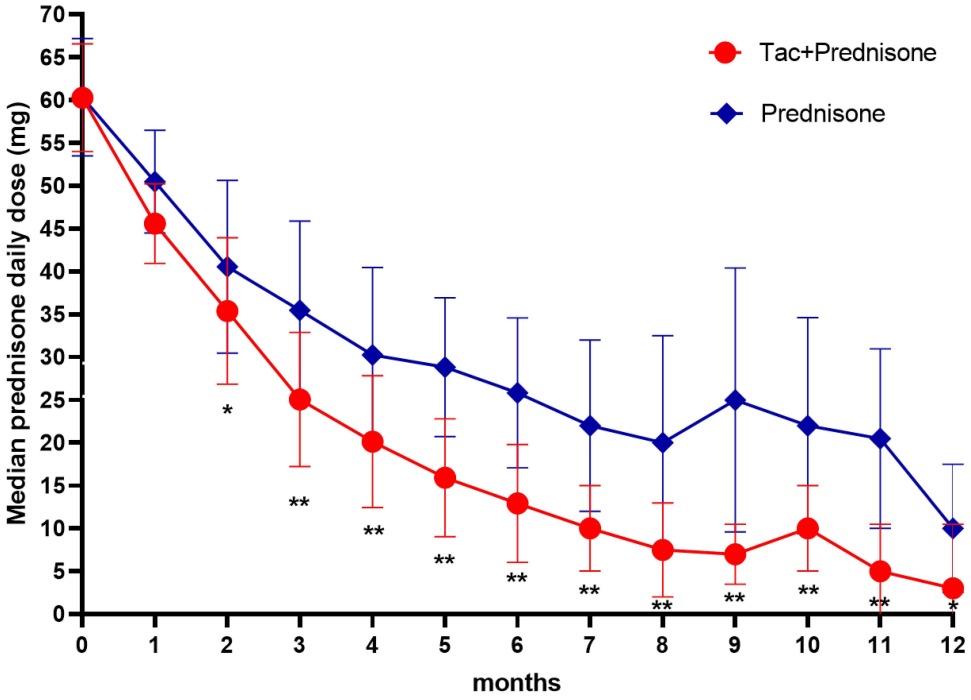

Figure 3 Comparison of the median daily prednisone dose between the tacrolimus plus prednisone (T&P) group and the prednisone monotherapy (PM) group in CIDP patients over the 12-month follow-up period. The median daily prednisone dose in the T&P group significantly lower than that in the PM group from the second month onward.
Notes: Due to the non-normal distribution of the data, the Mann–Whitney *U*-test was employed for statistical analysis. * $p<0.05$, ** $p<0.01$.
Abbreviation: Tac, tacrolimu.

(p = 0.04). More T&P patients achieved daily dose ≤5 mg at 12 months (56.3% [9/16] vs 16.7% [3/18]). Prednisone discontinuation rates were significantly higher in the T&P group over 12 months (43.8% [7/16] vs 11.1% [2/18]; p=0.001), with an overall discontinuation rate of 26.5% (9/34).

For tacrolimus, patients maintained a mean daily dose of 3.2±1.5 mg with trough concentrations of 5–10 ng/mL.

Safety Analysis

During the 12-month follow-up period, 15 of 34 patients (44.1%) remained free of adverse events (AEs). No single AE exceeded a 50% incidence rate in our cohort. Hyperglycemia was the most frequently reported adverse reaction in the T&P group, occurring in 37.5% (6/16) of patients, compared to 22.2% (4/18) in the PM group (Table 3). Affected patients in the T&P group exhibited an approximate 30% increase in both fasting and postprandial blood glucose levels, whereas elevations in the PM group were less pronounced. Hyperglycemia was managed through dietary counseling, initiation of oral hypoglycemic agents, and/or tacrolimus dose reduction. Dose reduction of tacrolimus demonstrated greater efficacy in glycemic control compared to prednisone dose reduction. No CTCAE Grade 3 or higher hyperglycemia-related events occurred, and no cases resulted in treatment discontinuation.

Tremor was the second common adverse reaction (25%, 4/16) in the T&P group, characterized by bilateral postural hand tremors that did not interfere with daily activities. Two patients in the PM group developed similar tremors. All cases were graded CTCAE Level 1, required no intervention, and gradually resolved with prednisone and tacrolimus tapering.

Elevated creatinine and urea nitrogen (BUN) were observed in two male patients over 60 years old, occurring 2–3 months after initiating tacrolimus. Both patients were asymptomatic, and the abnormalities were detected during routine laboratory testing. After reducing the tacrolimus dosage, both patients' creatinine and BUN levels returned to normal. One T&P-treated patient experienced self-limiting diarrhea during treatment initiation that resolved spontaneously without intervention.

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Table 3 Adverse Events in the Two Treatment Groups Over the 12-month Follow-up

Adverse Events, N (%)	T&P Group (N=16)	PM Group (N=18)
Elevated serum creatinine	2(12.5%)	0
Elevated serum urea nitrogen	2(12.5%)	0
Joint pain	2(12.5%)	0
Diarrhea	1(6.3%)	0
Tremor	4(25.0%)	2(11.1%)
Osteonecrosis of the femoral head	0	1(5.6%)
Hyperglycemia	6(37.5%)	4(22.2%)
Weight gain	2(12.5%)	8(44.4%)
Upper respiratory infection	0	1(5.6%)
Urinary tract infection	1(6.3%)	0
Onychomycosis	2(12.5%)	0
Folliculitis	1(6.3%)	3(16.7%)

Abbreviations: T&P, tacrolimus plus prednisone; PM, prednisone monotherapy.

Weight gain was the most frequently reported adverse reaction in the PM group (44.4%, 4/18), with a mean increase of approximately 5–10% in body weight, primarily manifesting as moon face and central obesity. The most severe adverse reaction in the PM group occurred in one patient who developed femoral head osteonecrosis, necessitating discontinuation of prednisone. Treatment was switched to tacrolimus monotherapy. During this period, CIDP symptoms showed no exacerbation, and the femoral head osteonecrosis was managed conservatively without surgical intervention.

No significant difference was observed in the overall incidence of infections between the two groups. In the T&P group, four patients (25%,4/16) developed infections: one urinary tract infection, two onychomycosis, and one folliculitis. Four patients (22%,4/18) in the PM group experienced infections, three folliculitis and one upper respiratory infection. All infectious events were CTCAE Grade 2, resolved with oral and topical medications, and did not require hospitalization.

Despite the occurrence of these adverse events, treatment compliance was not substantially compromised, as no patients discontinued the treatment regimen solely due to AEs. All adverse events were effectively managed through dose adjustments or concomitant medications.

Discussion

This retrospective study analyzed treatment responses in 34 CIDP patients who received either tacrolimus plus prednisone (T&P) or prednisone monotherapy (PM) as maintenance treatment. The results showed that the T&P group achieved earlier and more significant symptomatic improvement compared to the PM group. Moreover, the T&P regimen was associated with a significantly lower relapse rate (12.5% vs 33.3%), and a notable steroid-sparing effect beginning from the second month of treatment, and higher rates of successful prednisone withdrawal.

The first documented case demonstrating the benefits of tacrolimus in CIDP management was published by Ahlmén et al in 1998. It described a patient with relapsing-remitting CIDP who initially responded to high-dose prednisone but relapsed after discontinuation and proved refractory to IVIg, cyclophosphamide, and azathioprine. The addition of tacrolimus in combination with prednisone, the patient showed marked clinical improvement and was able to discontinue prednisone within one year.[18] More recent reports have further demonstrated the efficacy and safety of tacrolimus in two patients with typical CIDP[19] and nine with autoimmune nodopathies,[20] highlighting its role in preventing relapses and reducing corticosteroid dependence.

The 2021 EAN/PNS CIDP guidelines recommend azathioprine, mycophenolate mofetil, and cyclosporine as steroid-sparing agents.[6] However, to date, no randomized controlled trials (RCTs) investigating oral non-steroidal immunosuppressants in CIDP have reported positive results.[22] The first RCT, by Dyck et al in 1985, found no significant difference in disability scores between prednisolone alone and prednisolone plus azathioprine after nine months.[7] Similarly,

a randomized trial in 2009 reported no significant benefit from low-dose methotrexate for CIDP.[23] Studies evaluating cyclosporine and mycophenolate mofetil have been limited to case series and small retrospective analyses.[9,24,25] The largest cyclosporine study (n=19) showed improvement in 14 patients, but 11 experienced adverse effects including irreversible renal failure.[9] Tacrolimus and cyclosporine share a similar mechanism of action; tacrolimus is associated with a more favorable side effect profile. In the present study, transient elevations in creatinine/urea and hyperglycemia did occur but were effectively managed through dose adjustments and appropriate medical interventions.

Some studies reported that patients taking tacrolimus may develop symmetric bilateral pain in the lower extremities, typically involving the bones of the feet, ankles, and knees. The pain is often provoked by walking and standing, and symptoms such as allodynia and electric shock-like pain have also been described. This clinical presentation is defined as calcineurin inhibitor-induced pain syndrome (CIPS).[26] Diagnostic work-up is typically unremarkable, and differentiation from small fiber neuropathy is recommended. In this cohort, two patients developed bilateral knee soreness two months after initiating tacrolimus. The discomfort did not restrict their physical activity, and joint imaging revealed no abnormalities. No burning pain, trophic skin changes, or signs of vasomotor instability were observed. Consequently, comprehensive testing for small fiber neuropathy[27] was not pursued. In both cases, the tacrolimus dosage was reduced in response to elevated serum trough levels (13 ng/mL and 10.5 ng/mL, respectively), which was followed by spontaneous resolution of joint soreness.

The 2021 EAN/PNS guidelines recommend against the use of tacrolimus for CIDP, citing limited efficacy data and potential adverse effects.[6] Neurotoxicity is a well-documented concern for tacrolimus in transplant recipients,[28] often associated with high trough levels and specific risk factors such as hypomagnesemia, hypertension, and concurrent conditions. An 8-year prospective study of 1557 transplant recipients demonstrated that neurological impairment mainly occurred in patients who underwent immunosuppressant dosage reduction. This study identified pre-transplant polyneuropathy and reduced immunosuppressive intensity—rather than tacrolimus itself—as probable causative factors of post-transplant neuropathy.[29] The evidence of neurotoxicity in autoimmune neurological disorders remains scarce. Consistent with other studies using tacrolimus in CIDP,[18–20] the present study observed no worsening of neuropathy. These findings suggest a distinct risk profile for tacrolimus in CIDP patients compared to transplant recipients, likely attributable to differences in underlying immunopathogenic mechanisms between these patient populations.

The ADHERE trial demonstrated subcutaneous efgartigimod led to 67% clinical improvement and 61% reduced relapse risk versus placebo.[5] The T&P therapy also resulted in clinical improvement in 81.3% of CIDP patients and was associated with a reduced relapse rate (12.5% in the T&P group vs 33.3% in the PM group). With significantly lower costs compared to IVIg and efgartigimod, this regimen represents a promising treatment alternative for patients with limited financial resources.

Several limitations should be acknowledged. First, its retrospective, single-center design introduces inherent biases. More importantly, although this cohort represents the largest reported group of tacrolimus-treated CIDP patients to date, the sample size remains limited, resulting in insufficient statistical power for certain efficacy and safety outcomes. Therefore, large-scale, multicenter, prospective cohort studies or randomized controlled trials (RCTs) are warranted to further validate and generalize these findings. Second, the choice of induction therapy (methylprednisolone versus IVIg) was influenced by socioeconomic factors rather than randomization. Third, the dosing of both prednisone and tacrolimus during the maintenance phase was guided by clinical practice rather than standardized protocols, reflecting real-world treatment patterns.

The rarity of CIDP indeed poses a significant challenge to conducting large-scale RCTs, which represents a common difficulty in this field of research. This also underscores the value of our study from another angle—although the number of included patients is limited, the data collected provide a valuable and detailed real-world perspective of the treatment responses in this rare patient population. We believe that these findings can lay a foundation for future larger multicenter collaborative studies and offer insights for further optimizing clinical practice.

Furthermore, future studies should investigate the integration of pharmacogenetic testing with therapeutic drug monitoring (TDM) to develop combined algorithms for guiding initial dosing and subsequent titration, thereby optimizing treatment precision and improving individual outcomes.

Conclusion

This study provides real-world clinical evidence that tacrolimus plus prednisone therapy may contribute to improved symptom control, reduced relapse risk, and facilitated prednisone tapering in CIDP patients, while exhibiting a generally manageable safety profile. These findings support the potential role of tacrolimus as a corticosteroid-sparing agent in the CIDP management.

Ethics Approval and Informed Consent Statement

This study was approved by the Institutional Review Board of Xuanwu Hospital, Capital Medical University (No. 2023-235-003). All procedures were performed in accordance with the ethical principles in the Declaration of Helsinki. Written informed consent was obtained from all participants for inclusion in the Xuanwu Hospital CIDP database and for the use of their data in subsequent research. Patient confidentiality was rigorously protected throughout the study.

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Disclosure

The authors report no conflicts of interest in this work.

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