Subcutaneous immunoglobulin in CIDP and MMN: a short-term nationwide study.

Cocito D, Merola A, Peci E, Mazzeo A, Fazio R, Francia A, Valentino P, Liguori R, Filosto M, Siciliano G, Clerici AM, Lelli S, Marfia GA, Antonini G, Cecconi I, Nobile-Orazio E, Lopiano L

Subcutaneous immunoglobulin in CIDP and MMN: a short-term nationwide study.

JOURNAL OF NEUROLOGY (2014) 261

Subcutaneous immunoglobulin in CIDP and MMN: a short-term nationwide study

Dario Cocito[1], Aristide Merola[1], Erdita Peci[1], Anna Mazzeo[2], Raffaella Fazio[3], Ada Francia[4],Paola Valentino[5], Rocco Liguori[6], Massimiliano Filosto[7], Gabriele Siciliano[8], Angelo Maurizio Clerici[9],Stefania Lelli[10], Girolama Alessandra Marfia[11], Giovanni Antonini[12], Ilaria Cecconi[13], Eduardo Nobile-Orazio[14], Leonardo Lopiano[1] and SCIg and Chronic Dysimmune Neuropathies Italian Network

1. Department of Neuroscience, University of Turin, Via Cherasco 15, 10126 Turin, Italy
2. Department of Neuroscience, Psychiatry and Anesthesiology, A.O.U. Policlinico “G. Martino”, Messina, Italy
3. Department of Neurology, IRCCS San Raffaele Milano, Milano, Italy
4. III Neurological Clinic, Policlinico Umberto I, Roma, Italy
5. Department of Medical and Surgical Sciences, Neurological Clinic, University Magna Grecia of Catanzaro, Catanzaro, Italy
6. Neurological Clinic IRCCS, Institute of Neurological Sciences of Bologna, Bologna, Italy
7. Neuromuscular Diseases and Neuropathies Section, Neurological Clinic, University and A.O “Spedali Civili” of Brescia, Brescia, Italy
8. Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy
9. Neurology and Stroke Unit, A.O. Hospital Varese, Circolo and Fondazione Macchi, University of Insubria, Varese, Italy
10. Unit of Neurology, Hospital San Giacomo Apostolo, Castelfranco Veneto, Italy
11. Department of Neuroscience, Policlinico tor Vergata, Rome, Italy
12. Neurological Sciences, University “La Sapienza” of Rome, Rome, Italy
13. Child Neuropsychiatry Unit, Hospital Sant’Orsola Malpighi Bologna, Bologna, Italy
14. Neurology 2, Department of Translational Medicine, IRCCS Istituto Clinico Humanitas, University of Milano, Rozzano, Italy

Dario Cocito

Email: dariococito@yahoo.it

Received: 20 May 2014Revised: 14 July 2014Accepted: 15 July 2014Published online: 23 August 2014

Abstract

This multi-center Italian prospective observational study reports the 4 months follow-up data of 87 patients affected by chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multifocal motor neuropathy (MMN) shifted from intravenous to subcutaneous immunoglobulin treatment. A therapeutic shift from intravenous to subcutaneous immunoglobulin was performed in 87 patients (66 CIDP; 21 MMN) affected by immune-mediated peripheral neuropathies with evidence of a sustained clinical response to intravenous immunoglobulin. Patients were evaluated by means of the Overall Neuropathy Limitation Scale,Medical Research Council Scale and Life Quality Index questionnaire, both at the time of therapeutic shift and after 4 months of subcutaneous immunoglobulin treatment. A sustained clinical efficacy was observed after the switch to subcutaneous immunoglobulin: the Overall Neuropathy Limitation Scale score improved in the group of 66 CIDP patients (P = 0.018), with only one subject reporting a worsening of 1 point, and remained stable in the group of 21 MMN patients (P = 0.841), with one subject reporting a worsening of two points. An improvement in the patient's perception of therapeutic setting was reported in both groups. This large multi-center study confirms the short-term clinical equivalence of subcutaneous versus intravenous immunoglobulin and a possible improvement in the patient's perception of therapeutic setting with the subcutaneous administration. However, further studies are required to extend the results to a longer observational period.

Keywords

Chronic inflammatory demyelinating polyneuropathy Multifocal motor neuropathy Subcutaneous immunoglobulin Intravenous immunoglobulin Inflammatory neuropathy

Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multifocal motor neuropathy (MMN) are rare immune-mediated diseases presenting with progressive limb weakness and, in CIDP, also impaired sensory function. At the present time, intravenous immunoglobulin (IVIg) monthly infusions are the most recommended therapy, as it proved to stabilize the disease clinical progression and improve the isokinetic muscle strength [1, 2].

Moreover, the alternative option of subcutaneous immunoglobulin (SCIg) has been recently proposed, starting from the encouraging results observed in the primary immunodeficiency diseases, where an equal efficacy and a lower incidence of serious adverse events have been demonstrated [3]. The possible advantages of SCIg versus IVIg include a more stable plasmatic concentrations, lower emotional distress for the patient during infusion and a higher independence from the hospital care. In a double-blind randomized controlled clinical trial on 14 CIDP patients, Markvardsen et al. [4] observed that SCIg was well tolerated, with a significant improvement of isokinetic strength compared to placebo. In addition, Harbo et al. [5] reported a similar efficacy between subcutaneous and intravenous immunoglobulin in a cohort of MMN patients, and a commercial trial, investigating the efficacy of SCIg therapy in CIDP patients (PATH study), is currently ongoing.

Although the majority of clinical studies seems to suggest that SCIg could represent an effective alternative to IVIg, the literature data are still based on small single-center reports [4–11] and no official recommendation has been formulated yet.

In this context, we report here the results of a multi-center Italian prospective observational study, aiming to evaluate the SCIg therapy efficacy in the real-life setting of immune-mediated peripheral neuropathies treatment. A large sample of patients affected by CIDP and MMN were included in the analysis, reporting the main clinical and quality of life changes observed after the shift from intravenous to subcutaneous immunoglobulin, over a 4-month follow-up period.

Materials and methods

Patients

Patients from 12 Italian Neurological Departments and one Paediatric Neuropsychiatric Department were included in the study. Comorbidities that could by themselves cause neuropathy were excluded and all subjects fulfilled the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria for CIDP or MMN [1, 2]. At the time of recruitment, patients were in maintenance therapy with monthly IVIg infusions in two consecutive days, apart from one case, treated with a single-day intravenous infusion every 2 weeks (1 g/kg every 2 weeks).

All subjects reported a previous sustained response to IVIg therapy for ≥6 months and a "wear-off effect", defined as at least one of the following signs/symptoms between each immunoglobulin infusion: (a) worsening of fatigue; (b) increase of ≥1 point at the Overall Neuropathy Limitation Scale (ONLS); and (c) decrease of ≥1 point at the Medical Research Council (MRC) Scale.

IVIg doses, which were comprised between 1 and 2 g/kg monthly, were shifted to an equivalent SCIg dose (16 % solution of human IgG ready-to-use in 6 patients and 20 % solution of human IgG ready-to-use in 81 patients), administered in 1–3 subcutaneous infusions per week, according to each patient's total dose. The shift was performed after 5–10 days since the last intravenous infusion, at the maximal theoretical immunoglobulin efficacy. Subjects were instructed with their caregivers in subcutaneous self-administration and home infusion by a nurse experienced in this therapy; treatment was administered via a programmable infusion pump (chrono-speed 50 by Canè S.p.a., Italy) coupled to a 50 mL syringe connected with catheters to a butterfly subcutaneous needle. The ethical committee approval was obtained (CEI- 629 Prot. no 0010675, 25 Jan 2013) and all subjects signed a written informed consent.

Outcome measures

The primary study end-point was the maintenance of clinical efficacy with subcutaneous immunoglobulin, evaluated by the ONLS total score and the MRC muscle strength.

Secondary end-points were the evaluation and comparison of Life Quality Index (LQI) and side-effects profile with the two different therapeutic regimens.

Evaluation

Clinical assessments were performed at the time of switch to SCIg (T0 or baseline) and after 4 months of treatment (T1 or follow-up visit). Disability was assessed by means of the ONLS, while muscle strength was evaluated by means of MRC scale in eight muscle group bilaterally (shoulder abduction, elbow flexion, wrist extension, first dorsal interosseous, hip flexion, knee extension, and ankle flexion/extension) with a maximum score of 80 points. Quality of life measures and/or patient's preferences for one treatment over the other were compared by means of LQI, a validated scale used in previous SCIg trials [12]. LQI consists of 15 items examining the respondent's perceptions of immunoglobulin treatment impact on daily activities,

summarized to four sub-scales: “treatment interference”, “therapy-related problems”, “therapy setting”, and “treatment costs”. The symptom fatigue was assessed by means of a subjective clinical interview, without referring to specific scales.

Statistical evaluation

Descriptive statistics (mean, standard deviation, and range) were used for continuous variables, while categorical variables were described as percentages of subjects falling in each group. Wilcoxon non parametric test was used for comparison of follow-up data. All P values reported are two-tailed and a probability (P) value <0.05 was considered statistically significant. The analyses were performed using PASWStat 18 for Windows.

Results

Clinical follow-up data of 87 patients shifted from IVIg to SCIg between 2012 and 2014 were considered in the analyses: 66 were affected by CIDP and 21 by MMN (Table 1). The two groups were similar for age, disease duration, age at onset, gender distribution, and immunoglobulin total dose, with an IVIg infusion frequency of between 15 and 40 days, adapted to the single patient’s “wear-off” effect duration.

Table 1 Clinical and demographic characteristics of patients at baseline

	CIDP	MMN
Number of subjects	66	21
Age	56.7 ± 14.9	57.0 ± 14.6
	Range (12–84)	Range (31–79)
Gender		
Males	41	14
Females	25	7
Disease duration (years)	8.6 ± 6.0	8.9 ± 6.3
	Range (1.5–25)	Range (1.5–21)
Age at onset	48.6 ± 16.0	46.4 ± 14.1
	Range (10–79)	Range (23–71)
Subcutaneous immunoglobulin dose (g)	86.5 ± 32.7	86.6 ± 29.4
	Range (55–200)	Range (55–160)

CIDP Chronic inflammatory demyelinating polyradiculoneuropathy, *MMN* multifocal motor neuropathy

The ONLS total scores significantly improved in CIDP patients (Table 2) between T0 and T1 (P = 0.018), while no significant changes (P = 0.841) were observed in MMN patients (Table 3). An amelioration in the ONLS total score (at least 1 point) was observed in 33.3 % of CIDP patients, while 65.2 % remained stable and only one subject (1.5 %) worsened of 1 point. The majority of MMN patients (95.2 %) remained stable after the switch to SCIG, with only one subject worsening of two points at the ONLS total score. On the other hand, MRC score showed only a minimal improvement in CIDP patients (P = 0.342), and it remained substantially stable in MMN subjects (P = 0.950).

Table 2 CIDP patients: baseline versus follow-up data

	T0 (baseline)	T1 (4 months)	*P* value
Overall Neuropathy Limitation Scale	4.1 ± 2.8 Range (0–15)	3.1 ± 2.0 Range (0–10)	0.018
Medical Research Council Scale	69.9 ± 10.1 Range (40–80)	72.1 ± 9.0 Range (48–80)	0.342
Life Quality Index			
Sub-scale I	54.4 ± 21.1	91.5 ± 7.5	0.016
Sub-scale II	61.8 ± 14.2	87.7 ± 8.9	0.021
Sub-scale III	65.6 ± 24.0	96.6 ± 4.5	0.044
Sub-scale IV	34.8 ± 20.3	59.6 ± 10.2	0.071

Table 3 MMN patients: baseline versus follow-up data

	T0 (baseline)	T1 (4 months)	*P* value
Overall Neuropathy Limitation Scale	3.2 ± 1.6 Range (0–6)	3.3 ± 1.4 Range (1–6)	0.841
Medical Research Council Scale	73.3 ± 7.3 Range (60–80)	73.5 ± 6.9 Range (62–80)	0.950
Life Quality Index			
Sub-scale I	75.9 ± 9.2	87.6 ± 16.3	0.338
Sub-scale II	77.7 ± 3.1	87.5 ± 10.1	0.183
Sub-scale III	80.2 ± 7.9	96.8 ± 5.5	0.041
Sub-scale IV	50.0 ± 12.4	68.2 ± 3.8	0.071

Differences in patient's perception between the two therapeutic regimens were measured by means of the LQI scale (Tables 2, 3): LQI part-III subscores increased both in CIDP and MMN patients, indicating a patient's perception improvement in therapeutic setting, while LQI part-I and part-II improved only in the CIDP group, indicating an amelioration of treatment interference in the activities of daily living (P = 0.016) and in problems related to the administration of therapies (P = 0.021). Concerning the safety profile, SCIg was associated to a significantly lower incidence of adverse events: 21.8 % of patients (nineteen cases) reported side effects or adverse events during IVIg infusion, consisting of high blood pressure (eight cases), headache (eight cases), deep vein thrombosis (two cases), and nausea (one case). On the contrary, only one patient reported a significant adverse event during SCIg administration, consisting of a painful and itching cutaneous erythema that occurred 46 days after the start of treatment and required to return at IVIg for two courses. After the erythema resolution, SCIg therapy was reintroduced in another site of injection, without further complications.

Frequent and transient skin reactions (redness) without generalized symptoms, localized to the injection sites, were frequently observed and considered as an expectable reaction to subcutaneous infusion.

Discussion

This Italian nationwide unblinded multi-center study reports the clinical and quality of life data of a large sample of immune-mediated peripheral neuropathy patients, shifted from IVIg to SCIg. Subjects affected by CIDP and MMN, with evidence of active disease and reporting a "wear-off" effect between each IVIg administration, were evaluated at the time of shift to SCIg and then after 4 months of therapy. Safety reasons lead to choose a short follow-up duration, in view of the potential consequences of administering a less effective therapy in a large cohort of patients. Nevertheless, a follow-up duration of 4 months was considered adequate to highlight a possible lack of therapeutic efficacy [1, 2]. The main finding of this study was the maintenance of clinical efficacy with SCIg: only two patients (one CIDP and one MMN) worsened at the ONLS, while most subjects remained stable during follow-up and 22 CIDP patients showed an improvement.

SCIg administration was well tolerated: local minor side-effects (transient skin reactions) were frequently reported, but only one case required a temporary suspension because of a painful and itching erythema that completely disappeared in a few weeks.

Our findings confirm the results of previous smaller clinical reports [4–11], suggesting that SCIg could be considered as effective as IVIg in the treatment of chronic immune-mediated peripheral neuropathies. This might be relevant, since the clinical data currently reported in literature are still not clear and based on small cohorts of patients: Markvardsen et al. [4] observed a significant improvement in CIDP patients with SCIg and similar results have been also described by Harbo et al. [5, 9] in MMN subjects. On the other side, Eftimov et al. [8] did not observe any improvement after the shift from IVIg to SCIg, but only a clinical stability in four out of five subjects. In our cohort, we observed a possible different pattern of clinical response to SCIg between CIDP and MMN subjects: a significant improvement was observed in CIDP patients, both for clinical disability and LQI, with particular regard to the subscales related to "interference of the treatment with the activities of daily living" and to the "therapeutic setting". On the other hand, MMN patients remained substantially stable with SCIg, not reporting any improvement in disability scales and in muscle strength, with only a moderate amelioration in the LQI scores.

The two treatments have a different pharmacokinetics: IVIg infusion leads to an immediate increase of IgGplasmatic concentration, followed by a sharp decline within the first 2–8 days and a milder decrease in the following weeks [11]. The initial concentration plunge seems related to a shift from vascular to extracellular compartments [13], while the following mild decline might be due to immunoglobulin catabolism while returning to the vascular compartment. On the contrary, SCIg are adsorbed in the subcutaneous tissue and then gradually released, without significant peak of plasmatic concentrations [8].

It can be argued that differences in the pharmacokinetic profile might reflect in a differential therapeutic efficacy, however, the optimal dosage and frequency of immunoglobulin administration in chronic immune-mediated peripheral neuropathies are still not clear [14]. Some authors suggest that IVIg administration could be more effective, since a plasmatic threshold of IgG concentration should be reached, to obtain a clinical response [15, 16]. On the contrary, other authors [17] hypothesized that immunoglobulin therapeutic efficacy could be related to the reaching of a plasmatic concentration steady state, which can be achieved either after several IVIg infusions or with a constant subcutaneous delivery. Alternatively, it is also possible that anIgG plasmatic peak would be necessary to induce the initial improvement, but not to maintain the clinical stability [8].

Overall, in this large cohort of Italian patients, we observed an improvement of clinical disability in CIDP subjects and a substantial stability in MMN patients. It is possible that the more pronounced “wear-off” effect typical of MMN, or alternatively the lack of IgG plasmatic peak of intravenous administration, accounted for part of these differences. However, other possible explanations might be related to the disability scales used for evaluations: the ONLS improvement observed in CIDP patients could be partly related to sensory functions tasks, which are not affected in MMN, like “turn a key in a lock” or “do or undo buttons or zip”. The effect of SCIg could have been therefore underestimated in MMN patients, while the use of a more specific scale, as the Rasch-built Overall Disability Scale [18], may lead to different results.

In conclusion our findings suggest that SCIg therapy seems to have a similar clinical efficacy than IVIg, with a lower profile of side-effects. Moreover SCIg requires lower resources [19, 20] in terms of direct costs (drugs for pre-medication, health care professional time) and indirect costs, such as loss of working time for the patient/caregiver, transport and parking (IVIg administration at the patient’s domicile is not allowed in Italy).

However, given the lack of a control group and the short follow-up duration, we can not assert the superiority of one treatment over the other, even if a clinical and LQI amelioration was observed in the group of CIDP patients. On the other hand, our findings seems to confirm the short-term follow-up safety and effectiveness of SCIg in patients responders to IVIg. These data may be particularly relevant for patients without a valid peripheral venous access, or experiencing adverse events with IVIg infusion or having difficulties in reaching the hospital.

Further studies, with a longer follow-up duration seems necessary to confirm our results, the long term efficacy of SCIg and the possible differences in the therapeutic response between CIDP and MMN patients.

Conflicts of interest

This research was funded by the “Associazione Neuropatie Croniche Piemonte ONLUS”. The sponsor had no role in the design of the study; the collection, analysis and interpretation of the data; the decision to approve publication of the finished manuscript. Dario Cocito received honoraria for lecturing from Baxter, CSL Behring, and Kedrion; he received personal compensation for serving in Advisory Board of CSL Behring, Kedrion and Lilly and travel grants to attend scientific meeting from Baxter, Grifols, Kedrion, and CSL Behring. Anna Mazzeo reports travel support for Scientific Meetings from CSL Behring and Kedrion. Raffaella Fazio received personal compensation for serving in Advisory Board of CSL Behring and Baxter, and travel grants from Baxter, Grifols, Kedrion and CLS Behring. Ada Francia received travel grants and honoraria from Biogenidec, Genzyme, Novartis, Almirall, Merck Serono, CSL Behring, Kedrion, Teva. Gabriele Siciliano received personal compensation for serving in Advisory Board from Grunenthal, Baxter and Grifols. Giovanni Antonini received honoraria for lecturing from Kedrion and travelgrant from Genzyme, Behring e Kedrion. Eduardo Nobile-Orazio reports personal compensation for serving in the Advisory Board of CSL Behring, Baxter, Kedrion and Novartis; he received honoraria for lecturing travel grants to attend scientific meetings from Baxter, CSL Behring, Grifols and Kedrion. Erdita Peci, Girolama Alessandra Marfia received travel grant to attend scientific meetings from CSL Behring. Aristide Merola, Paola Valentino, Rocco Liguori, Massimiliano Filosto, Angelo Maurizio Clerici, Stefania Lelli, Ilaria Cecconi, and Leonardo Lopiano declare no conflicts of interest.

Ethical standards

The authors declare that they acted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

References

1. Van den Bergh PY, Hadden RD, Bouche P, Cornblath DR, Hahn A, Illa I et al (2010) European Federation of Neurological Societies; Peripheral Nerve Society. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society—first revision. Eur J Neurol 17:356–363PubMedCrossRef
2. Joint Task Force of the EFNS and the PNS (2010) European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society—first revision. J Peripher Nerv Syst 15:295–301CrossRef
3. Gardulf A, Hammarstrom L, Smith CL (1991) Home treatment of hypogammaglobulinemia with subcutaneous gammaglobulin by rapid infusion. Lancet 338:162–166PubMedCrossRef
4. Markvardsen LH, Debost JC, Harbo T, Sindrup SH, Andersen H, Christiansen I et al (2013) Subcutaneous immunoglobulin in responders to intravenous therapy with chronic inflammatory demyelinating polyradiculoneuropathy. Eur J Neurol 20:836–842PubMedCrossRef
5. Harbo T, Andersen H, Hess A, Hansen K, Sindrup SH, Jakobsen J (2009) Subcutaneous versus intravenous immunoglobulin in multifocal motor neuropathy: a randomized, single-blinded cross-over trial. Eur J Neurol 16:631–638PubMedCrossRef
6. Köller H, Schroeter M, Feischen H, Hartung HP, Kieseier BC (2006) Subcutaneous self-infusions of immunoglobulins as a potential therapeutic regimen in immune-mediated neuropathies. J Neurol 253:1505–1506PubMedCrossRef
7. Lee DH, Linker RA, Paulus W, Schneider-Gold C, Chan A, Gold R (2008) Subcutaneous immunoglobulin infusion: a new therapeutic option in chronic inflammatory demyelinating polyneuropathy. Muscle Nerve 37:406–409PubMedCrossRef
8. Eftimov F, Vermeulen M, de Haan RJ, van den Berg LH, van Schaik IN (2009) Subcutaneous immunoglobulin therapy for multifocal motor neuropathy. J Peripher Nerv Syst 14:93–100PubMedCrossRef
9. Harbo T, Andersen H, Jakobsen J (2010) Long-term therapy with high doses of subcutaneous imunoglobulin in multifocal motor neuropathy. Neurology 75:1377–1380PubMedCrossRef
10. Cocito D, Serra G, Falcone Y, Paolasso I (2011) The efficacy of subcutaneous immunoglobulin administration in chronic inflammatory demyelinating polyneuropathy responders to intravenous immunoglobulin. J Peripher Nerv Syst 16:150–152PubMedCrossRef
11. Misbah SA, Baumann A, Fazio R, Dacci P, Schmidt DS, Burton J et al (2011) A smooth transition protocol for patients with multifocal motor neuropathy going from intravenous to subcutaneous immunoglobulin therapy: an open-label proof-of-concept study. J Peripher Nerv Syst 16:92–97PubMedCrossRef
12. Nicolay U, Kiessling P, Berger M, Gupta S, Yel L, Roifman CM et al (2006) Health-related quality of life and treatment satisfaction in North American patients with primary immunedeficiency diseases receiving subcutaneous IgG self-infusions at home. J Clin Immunol 26:65–72PubMedCrossRef

13. Boërio D, Créange A, Hogrel JY, Guéguen A, Bertrand D, Lefaucheur JP (2010) Nerve excitability changes after intravenous immunoglobulin infusions in multifocal motor neuropathy and chronic inflammatory demyelinating neuropathy. J Neurol Sci 292:63–71PubMedCrossRef
14. Rajabally YA (2013) Subcutaneous immunoglobulin therapy for inflammatory neuropathy: current evidence base and future prospects. J Neurol Neurosurg Psychiatry. doi:10.1136/jnnp-2013-305644PubMed
15. Van Doorn PA, Kuitwaard K, Jacobs BC (2011) Serum IgG levels as biomarkers for optimizing IVIg therapy in CIDP. J Peripher Nerv Syst 16:38–40PubMedCrossRef
16. Vlam L, Cats EA, Willemse E, Franssen H, Medic J, Piepers S et al (2013) Pharmacokinetics of intravenous immunoglobulin in multifocal motor neuropathy. J Neurol Neurosurg Psychiatry. doi:10.1136/jnnp-2013-306227PubMed
17. Kuitwaard K, van Doorn PA, Vermeulen M, van den Berg LH, Brusse E, van der Kooi AJ et al (2013) Serum IgG levels in IV immunoglobulin treated chronic inflammatory demyelinating polyneuropathy. J Neurol Neurosurg Psychiatry 84:859–861PubMedCrossRef
18. Van Nes SI, Vanhoutte EK, van Doorn PA, Hermans M, Bakkers M, Kuitwaard K et al (2011) Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies. Neurology 76:337–345PubMedCrossRef
19. Cocito D, Serra G, Paolasso I, Barilà DA, Lopiano L, Cattel L (2012) Economic and quality of life evaluation of different modalities of immunoglobulin therapy in chronic dysimmune neuropathies. J Peripher Nerv Syst 17:426–428PubMedCrossRef
20. Lazzaro C, Lopiano L, Cocito D (2014) Subcutaneous vs Intravenous administration of immunoglobulin in chronic inflammatory demyelinating polyneuropathy: an Italian cost-minimization analysis. Neurol Sci 35:1023–1034