CADTH

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Off-Label Use of Intravenous Immunoglobulin for Neurological Conditions: Clinical Effectiveness

Service Line: Rapid Response Service
Version: 1.0
Publication Date: October 30, 2017
Report Length: 15 Pages

CADTH

Authors: Kelsey Seal, Sarah Visintini

Cite As: Off-Label Use of Intravenous Immunoglobulin for Neurological Conditions: Clinical Effectiveness. Ottawa: CADTH; 2017 Oct. (CADTH rapid response report: summary of abstracts).

Acknowledgments:

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Research Question

What is the clinical effectiveness of the off-label use of intravenous immunoglobulin for the treatment of neurological or neuromuscular conditions?

Key Findings

Sixteen systematic reviews (five with meta-analyses), 10 randomized controlled trials, and seven non-randomized studies were identified regarding the clinical effectiveness of off-label use of intravenous immunoglobulin for the treatment of neurological or neuromuscular conditions.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and October 17, 2017. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients any age with neurological or neuromuscular conditions that are not approved indications for IVIG, including but not limited to: • Acute disseminated encephalomyelitis • Acute idiopathic dysautonomia • Bickerstaff encephalitis • Central nervous system vasculitis • Cerebral infarction with antiphospholipid antibodies • Chronic inflammatory demyelinating polyneuropathy • Chronic regional pain syndrome (CRPS) • Eaton-Lambert myasthenic syndrome • Myasthenia Gravis • Neuromyotonia • Paraproteinaemic demyelinating neuropathy • Relapsing-remitting multiple sclerosis • Stiff person syndrome
Intervention	Human IVIG or SCIG products, including but not limited to those available in Canada, alone or in combination with corticosteroids or other immunomodulation therapy.
Comparators	Treatment as usual; Placebo; No treatment
Outcomes	Clinical benefits and harms
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Sixteen systematic reviews (five with meta-analyses), 10 randomized controlled trials, and seven non-randomized studies were identified regarding the clinical effectiveness of off-label use of intravenous immunoglobulin for the treatment of neurological or neuromuscular conditions. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Sixteen systematic reviews (SRs)[1-16] (five with meta-analyses[1,7,10-12]), 10 randomized controlled trials[17-26], and seven non-randomized studies[27-33] were identified regarding the clinical effectiveness of off-label use of intravenous immunoglobulin for the treatment of neurological or neuromuscular conditions. Intravenous immunoglobulin has been used for a wide variety of neurological and neurodevelopmental conditions. Twenty-two studies[1-2,4-6,10,13-15,18-19, 22-28,30-33] were favourable to the use of intravenous immunoglobulin for certain

conditions, eight studies[3,8,11-12,16-17,20-21] did not form a conclusion or were neutral due to insufficient data or the non-superiority of the drug when compared to placebo or active comparator, one SR[9] reported that intravenous immunoglobulin had some benefit in the short term, one SR[7] found comparable results between subcutaneous immunoglobulin and intravenous immunoglobulin, and one non-randomized study[29] concluded that plasmapheresis was a safe treatment in comparison to intravenous immunoglobulin. Detailed study characteristics and study conclusions are provided in Table 2.

Table 2: Summary of Included Studies on the Clinical Effectiveness of Off-Label Use of Intravenous Immunoglobulin for the Treatment of Neurological or Neuromuscular Conditions

First Author, Year	Study Characteristics	Neurological or Neuromuscular Condition	Intervention, Comparator	Outcomes	Conclusions
Systematic Reviews and Meta-Analyses					
Al Amrani, 2017[1]	• MA performed • 4 included studies • N=8 • Patients aged 0-18 years	• Intractable epilepsy secondary to focal cortical dysplasia	• IVIG • No comparator	• Reduction of seizure frequency	• IVIG may be an effective treatment of intractable epilepsy secondary to focal cortical dysplasia
Gadian, 2017[2]	• 65 included studies • Pediatric patients (age not specified)	• Neurological and neurodevelop-mental disorders including GB and CIDP	• IVIG • No comparator, cortico-steroids (in GB)	• Recovery time • Effectiveness	• IVIG is a useful therapy in selected conditions • IVIG reduced recovery time in GB • IVIG was as effective as corticosteroids in treating CIDP
Geng, 2017[3]	• 1 included RCT	• Epilepsy	• IVIG • Placebo	• Seizure-free • Reduction in seizures • Adverse effects • Treatment withdrawal • QoL	• No conclusions can be drawn regarding the efficacy of IVIG as a treatment for epilepsy
Gernigon, 2017[4]	• NR	• 28 different neurological indications	• IVIG • Placebo • No comparator	• Efficacy • Safety	• IVIGs were found to be efficacious in RCTs in the following indications: CIDP and GB (high level of evidence), MMF(moderate level of evidence), dermatomyositis, MG, polymyositis, RRMS, stiff person syndrome, and Lambert-Eaton myasthenic syndrome (low quality) • IVIGs were not more efficacious than placebo or no intervention in

Table 2: Summary of Included Studies on the Clinical Effectiveness of Off-Label Use of Intravenous Immunoglobulin for the Treatment of Neurological or Neuromuscular Conditions

First Author, Year	Study Characteristics	Neurological or Neuromuscular Condition	Intervention, Comparator	Outcomes	Conclusions
					adrenoleukodystrophy, AD, inclusion body myositis, and progressive-secondary multiple sclerosis
Gogou, 2017[5]	• 11 included studies Pediatric patients (age not specified)	• Drug-resistant epilepsy • encephalitis	• IVIG • NR	• Adverse events	• Administration of IVIG could be justified in child epilepsy
Iro, 2017[6]	• 3 included RCTs • N=138 • Pediatric patients (age not specified)	• Encephalitis	• IVIG • Standard care • Placebo	• Safety • Efficacy	• There may be a clinical benefit of adjunctive IVIG treatment for children with viral encephalitis for some clinical measures
Racosta, 2017[7]	• MA performed • 8 included studies • N = 138	• MMF • CIDP	• IVIG • SCIG	• Safety • Efficacy	• SCIG was similar in efficacy to IVIG and has a significant safety profile
Zeiler, 2017[8]	• 24 included studies • N=33	• Refractory status epilepticus	• IVIG • NR	• Seizure control • Seizure reduction	• There was an unclear impact of IVIG in adults with refractory status epilepticus
Lunn, 2016[9]	• 8 included trials • N=236	• Demyelinating peripheral neuropathy	• IVIG • NR	• Efficacy	• IVIG has statistically significant, but likely not clinically significant, benefit in the short term
Olyaeemaneshh, 2016[10]	• MA performed • 6 included trials • N=537	• RRMS	• IVIG • Comparison	• Safety • Efficacy	• IVIG may be an alternative therapeutic option, second-line therapy or adjuvant therapy due to its beneficial effects (high tolerance, need to be injected with longer intervals)
Ortiz-Salas, 2016[11]	• MA performed • 24 included studies • N=4657	• MGGB	• IVIG • PE	• Safety • Efficacy	• No superiority in efficacy or safety was established for IVIG or PE in the management of MG or GB
Huang, 2015[12]	• MA performed • 8 included studies • N=508	• PPS	• IVIG • Placebo	• Pain severity • Fatigue scores • Muscle strength • Physical performance	• IVIG was unlikely to produce significant improvements in pain, fatigue, or muscle strength

Table 2: Summary of Included Studies on the Clinical Effectiveness of Off-Label Use of Intravenous Immunoglobulin for the Treatment of Neurological or Neuromuscular Conditions

First Author, Year	Study Characteristics	Neurological or Neuromuscular Condition	Intervention, Comparator	Outcomes	Conclusions
				• QoL • Cytokine expression levels	
Koopman, 2015[13]	• 10 included pharmacological studies (including IVIG) • N=675 (including IVIG studies)	• PPS	• IVIG • NR	• Self-perceived activity limitations • Muscle strength • Muscle endurance • Fatigue • Pain • Adverse events	• IVIG may be beneficial, but needs further investigation to see if any real and meaningful effect exists
Vitaliti, 2015[14]	• Pediatric patients (age not specified)	• Neuro-degenerative disorders	• IVIG • PE	• Efficacy	• IVIG was found to be efficient in the treatment of post-streptococcal neurodegenerative disorders
Hughes, 2014[15]	• 12 included trials	• GB in adult and pediatric patients	• IVIG • PE • Active comparators	• Efficacy	• One trial (N=21) examining pediatric patients found significant improvements in disability grade after four weeks with IVIG than with support treatment alone
Gajdos, 2012[16]	• 7 included RCTs	• MG	• IVIG • Placebo • PE	• Efficacy	• There is insufficient evidence from RCTs to determine whether IVIG in efficacious in patients with chronic myasthenia gravis
Randomized Controlled Trials					
Absoud, 2017[17]	• N=2 • Adults and children	• Transverse myelitis • Neuromyelitis optica	• IVIG • Standard treatment	• Efficacy	• The effect of IVIG could not be determined because the study did not reach an endpoint
Alipour-Faz, 2017[18]	• N=24	• MG	• IVIG • PE	• Efficacy	• The administration of IVIG may be more effective in preparation before thymectomy in patients with MG
Kile, 2017[19]	• N=50 • 50-84 years of	• AD	• IVIG • Placebo	• Efficacy	• A short course of IVIG in the mild cognitive impairment

Table 2: Summary of Included Studies on the Clinical Effectiveness of Off-Label Use of Intravenous Immunoglobulin for the Treatment of Neurological or Neuromuscular Conditions

First Author, Year	Study Characteristics	Neurological or Neuromuscular Condition	Intervention, Comparator	Outcomes	Conclusions
	age				stage reduces brain atrophy, prevents cognitive decline, and delays conversion to dementia, however, this effect appears to wane by 2 years
Relkin, 2017[20]	• N=390	• AD	• IVIG • Placebo	• Efficacy • Safety • Tolerability data	• Patients with mild to moderate AD showed good tolerability of IVIG treatment, but did not show beneficial effects on cognition or function relative to participants who received placebo
Van Klink, 2016[21]	• N=66 • Pediatric patients (age not specified)	• Rhesus hemolytic disease	• IVIG • Placebo	• Incidence of neurodevelop-mental impairment	• The long-term neurodevelopmental outcome in children treated with IVIG was not different then children treated with placebo
Rayamajhi, 2015[22]	• N=22 • Pediatric patients (age not specified)	• Japanese encephalitis	• IVIG • Placebo	• Efficacy	• IVIG may be an appealing option for treatment in patients with Japanese encephalitis
Bertolasi, 2013[23]	• N=51	• PPS	• IVIG • Placebo	• Health-related quality of life • Muscle strength	• Although the study did not reach a primary endpoint, a single IVIG course improved health-related quality of life
Dodel, 2013[24]	• N=55 • 50-85 years of age	• AD	• IVIG • Placebo	• Safety • Effective dose	• IVIG may have an acceptable safety profile
Hahn, 2013[25]	• N=44	• MMF	• IVIG • Placebo	• Safety • Efficacy	• IVIG was effective in improving disability and muscle strength; it was also safe and well tolerated
Jann, 2012[26]	• N=20	• Refractory neuropathic pain	• IVIG • Previous therapy	• Pain • QoL	• IVIG showed a beneficial effect on neuropathic pain intensity and quality of life
Non-Randomized Studies					
Beecher, 2017[27]	• N=22 • ≥ 18 years • Prospective	• MG	• SCIG • NR	• Efficacy • Safety	• SCIG was safe and effective in mild to moderate MG
Nobile-	• N=20 • Retrospective	• MMF	• IVIG • NR	• Efficacy	• High-dose IVIG is efficacious and well tolerated

Table 2: Summary of Included Studies on the Clinical Effectiveness of Off-Label Use of Intravenous Immunoglobulin for the Treatment of Neurological or Neuromuscular Conditions

First Author, Year	Study Characteristics	Neurological or Neuromuscular Condition	Intervention, Comparator	Outcomes	Conclusions
Orazio, 2017[28]					
Parra-Salinas, 2017[29]	• N=26 • Retrospective	• Peripheral polyneuropathy and central nervous system acute inflammatory disease	• IVIG • Plasma-pheresis	• Efficacy	• Plasmapheresis was safe, but more studies are needed to determine the benefit for long-term outcome
Liew, 2014[30]	• N=54 • Pediatric patients (age not specified) • Retrospective	• MG	• IVIG • Plasma-pheresis	• Efficacy	• Both IVIG and plasmapheresis have high response rates as maintenance therapies
Barnett, 2013[31]	• N=62 • Follow-up study	• MG	• IVIG • Plasma-pheresis	• QoL	• IVIG and plasmapheresis are comparable in the treatment of patients with moderate to severe myasthenia gravis
Gonzalez, 2012[32]	• N=41 • Follow-up study	• PPS	• IVIG • Placebo	• QoL	• IVIG had effects on quality of life variables up to one year in patients with postpolio syndrome
Novak, 2012[33]	• N=9 • 55-64 years of age • Prospective	• Multiple system atrophy	• IVIG • None	• Safety • Efficacy	• IVIG appears to be safe, feasible and may improve functionality

AD = Alzheimer's disease; CIDP = Chronic Inflammatory Demyelinating Polyradiculoneuropathy; GB = Guillain-Barre Syndrome; IVIG = intravenous immunoglobulin; MA = meta-analysis; MG = Myasthenia Gravis; MMF = multifocal motor neuropathy; NR = not reported; PE = plasma exchange; PPS = Postpolio syndrome; QoL = quality of life; RCT = randomized controlled trial; RRMS = relapsing remitting multiple sclerosis; SCIG = subcutaneous immunoglobulin; SR = systematic review.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Al Amrani F, Dudley R, Bello-Espinosa LE, Rosenblatt B, Srour M, Sebire G. Intravenous immunoglobulin as a treatment for Intractable epilepsy secondary to focal cortical dysplasia: A meta-analysis. Pediatr Neurol. 2017 Jul 19. PubMed: PM28969879

2. Gadian J, Kirk E, Holliday K, Lim M, Absoud M. Systematic review of immunoglobulin use in paediatric neurological and neurodevelopmental disorders. Dev Med Child Neurol. 2017 Feb;59(2):136-44. PubMed: PM27900773

3. Geng J, Dong J, Li Y, Ni H, Jiang K, Shi LL, Wang G. Intravenous immunoglobulins for epilepsy. Cochrane Database of Systematic Reviews [Internet] 2017 [cited 2017 Oct 26];7:CD008557. Available from : http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008557.pub3/full

4. Institut national d'excellence en santé et en services sociaux (INESSS), Gernigon G, Guay H, Breton M-C. Usage optimal des immunoglobulins en neurologie. ETMIS [Internet]. 2017 [cited 2017 Oct 26]. Available from: http://www.inesss.qc.ca/nc/publications/publications/publication/usage-optimal-des-immunoglobulines-en-neurologie.html

5. Gogou M, Papadopoulou-Alataki E, Spilioti M, Alataki S, Evangeliou A. Clinical applications of intravenous immunoglobulins in child neurology. Curr Pharm Biotechnol. 2017 Sep 15. PubMed: PM28914199

6. Iro MA, Martin NG, Absoud M, Pollard AJ. Intravenous immunoglobulin for the treatment of childhood encephalitis. Cochrane Database Syst Rev. 2017;10: CD011367. PubMed: PM28967695

7. Racosta JM, Sposato LA, Kimpinski K. Subcutaneous versus intravenous immunoglobulin for chronic autoimmune neuropathies: A meta-analysis. Muscle Nerve. 2017 Jun;55(6):802-9. PubMed: PM27649063

8. Zeiler FA, Matuszczak M, Teitelbaum J, Kazina CJ, Gillman LM. Intravenous immunoglobulins for refractory status epilepticus, part I: A scoping systematic review of the adult literature. Seizure. 2017 Feb;45:172-80. PubMed: PM28068584

9. Lunn MP, Nobile-Orazio E. Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies. Cochrane Database Syst Rev. 2016;10:CD002827. PubMed: PM27701752

10. Olyaeemanesh A, Rahmani M, Goudarzi R, Rahimdel A. Safety and effectiveness assessment of intravenous immunoglobulin in the treatment of relapsing-remitting multiple sclerosis: A meta-analysis. Med J Islam Repub Iran [Internet]. 2016 [cited 2017 Oct 26];30:336. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4898867 PubMed: PM27390706

11. Ortiz-Salas P, Velez-Van-Meerbeke A, Galvis-Gomez CA, Rodriguez QJ. Human immunoglobulin versus plasmapheresis in Guillain-Barre syndrome and myasthenia gravis: A meta-analysis. J Clin Neuromuscul Dis. 2016 Sep;18(1):1-11. PubMed: PM27552383

12. Huang YH, Chen HC, Huang KW, Chen PC, Hu CJ, Tsai CP, et al. Intravenous immunoglobulin for postpolio syndrome: a systematic review and meta-analysis. BMC Neurol. [Internet] 2015 Mar 22 [cited 2017 Oct 26];15:39. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4379590 PubMed: PM25886512

13. Koopman FS, Beelen A, Gilhus NE, de VM, Nollet F. Treatment for postpolio syndrome. Cochrane Database Syst Rev. 2015 May 18;(5):CD007818. PubMed: PM25984923

14. Vitaliti G, Tabatabaie O, Matin N, Ledda C, Pavone P, Lubrano R, et al. The usefulness of immunotherapy in pediatric neurodegenerative disorders: A systematic review of literature data. Hum Vaccin Immunother [Internet]. 2015 [cited 2017 Oct 26];11(12):2749-63. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5391617 PubMed: PM26266339

15. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barre syndrome. Cochrane Database Syst Rev. 2014 Sep 19;(9):CD002063. PubMed: PM25238327

16. Gajdos P, Chevret S, Toyka KV. Intravenous immunoglobulin for myasthenia gravis. Cochrane Database Syst Rev. 2012 Dec 12;12:CD002277. PubMed: PM23235588

Randomized Controlled Trials

17. Absoud M, Brex P, Ciccarelli O, Diribe O, Giovannoni G, Hellier J, et al. A multicentre randomised controlled trial of Intravenous immunoglobulin compared with standard therapy for the treatment of transverse myelitis in adults and children (STRIVE). Health Technol Assess [Internet]. 2017 [cited 2017 Oct 26] May;21(31):1-50. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5512007 PubMed: PM28639937

18. Alipour-Faz A, Shojaei M, Peyvandi H, Ramzi D, Oroei M, Ghadiri F, et al. A comparison between IVIG and plasma exchange as preparations before thymectomy in myasthenia gravis patients. Acta Neurol Belg. 2017 Mar;117(1):245-9. PubMed: PM27530310

19. Kile S, Au W, Parise C, Rose K, Donnel T, Hankins A, et al. IVIG treatment of mild cognitive impairment due to Alzheimer's disease: a randomised double-blinded exploratory study of the effect on brain atrophy, cognition and conversion to dementia. J

Neurol Neurosurg Psychiatry. 2017 Feb;88(2):106-12.
PubMed: PM26420886

20. Relkin NR, Thomas RG, Rissman RA, Brewer JB, Rafii MS, van Dyck CH, et al. A phase 3 trial of Iv immunoglobulin for Alzheimer disease. Neurology [Internet]. 2017 May 2 [cited 2017 Oct 26];88(18):1768-75. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5409846
PubMed: PM28381506

21. van Klink JM, van Veen SJ, Smits-Wintjens VE, Lindenburg IT, Rijken M, Oepkes D, et al. Immunoglobulins in neonates with rhesus hemolytic disease of the fetus and newborn: long-term outcome in a randomized trial. Fetal Diagn Ther. 2016;39(3):209-13.
PubMed: PM26159803

22. Rayamajhi A, Nightingale S, Bhatta NK, Singh R, Kneen R, Ledger E, et al. A preliminary randomized double blind placebo-controlled trial of intravenous immunoglobulin for Japanese encephalitis in Nepal. PLoS ONE [Internet]. 2015 [cited 2017 Oct 26];10(4):e0122608. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4401695
PubMed: PM25886645

23. Bertolasi L, Frasson E, Turri M, Gajofatto A, Bordignon M, Zanolin E, et al. A randomized controlled trial of Iv immunoglobulin in patients with postpolio syndrome. J Neurol Sci. 2013 Jul 15;330(1-2):94-9.
PubMed: PM23683859

24. Dodel R, Rominger A, Bartenstein P, Barkhof F, Blennow K, Forster S, et al. Intravenous immunoglobulin for treatment of mild-to-moderate Alzheimer's disease: a phase 2, randomised, double-blind, placebo-controlled, dose-finding trial. Lancet Neurol [Internet]. 2013 Mar [cited 2017 Oct 26];12(3):233-43. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4986921
PubMed: PM23375965

25. Hahn AF, Beydoun SR, Lawson V, IVIG in MMN Study Team, Oh M, Empson VG, et al. A controlled trial of intravenous immunoglobulin in multifocal motor neuropathy. J Peripher Nerv Syst. 2013 Dec;18(4):321-30.
PubMed: PM24725024

26. Jann S, Francia A, Fruguglietti ME, De Toni FL, Sterzi R. Efficacy and safety of intravenous immunoglobulin as adjuvant treatment for refractory neuropathic pain. Results of an open-label, multicenter study. Pain Med. 2012 Oct;13(10):1334-41.
PubMed: PM22958476

Non-Randomized Studies

27. Beecher G, Anderson D, Siddiqi ZA. Subcutaneous immunoglobulin in myasthenia gravis exacerbation: A prospective, open-label trial. Neurology. 2017 Sep 12;89(11):1135-41.
PubMed: PM28814461

28. Nobile-Orazio E, Cocito D, Briani C, Plasmati R, Schenone A, Gallia F, et al. High-dose Ig VENA is well tolerated and efficacious in patients with multifocal motor neuropathy.

Neurol Sci. 2017 May;38(5):899-902.
PubMed: PM28144763

29. Parra-Salinas I, Gonzalez-Rodriguez VP, Gracia Pina JA, Gimeno Lozano JJ, Garcia-Erce JA. Benefit in long-term response and mortality of treatment with intravenous immunoglobulin prior to plasmapheresis in peripheral polyneuropathies. Transfus Clin Biol. 2017 Feb;24(1):9-14.
PubMed: PM27865608

30. Liew WK, Powell CA, Sloan SR, Shamberger RC, Weldon CB, Darras BT, et al. Comparison of plasmapheresis and intravenous immunoglobulin as maintenance therapies for juvenile myasthenia gravis. JAMA Neurol. 2014 May;71(5):575-80.
PubMed: PM24590389

31. Barnett C, Wilson G, Barth D, Katzberg HD, Bril V. Changes in quality of life scores with intravenous immunoglobulin or plasmapheresis in patients with myasthenia gravis. J Neurol Neurosurg Psychiatry. 2013 Jan;84(1):94-7.
PubMed: PM23154126

32. Gonzalez H, Khademi M, Borg K, Olsson T. Intravenous immunoglobulin treatment of the post-polio syndrome: sustained effects on quality of life variables and cytokine expression after one year follow up. J Neuroinflammation [Internet]. 2012 Jul 9 [cited 2017 Oct 26];9:167. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3464723
PubMed: PM22776106

33. Novak P, Williams A, Ravin P, Zurkiya O, Abduljalil A, Novak V. Treatment of multiple system atrophy using intravenous immunoglobulin. BMC Neurol [Internet]. 2012 Nov 1 [cited 2017 Oct 26];12:131. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3551813
PubMed: PM23116538

Appendix — Further Information

Systematic Reviews and Meta-Analysis – Approved Indications

34. Oaklander AL, Lunn MP, Hughes RA, van Schaik I, Frost C, Chalk CH. Treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): an overview of systematic reviews. Cochrane Database Syst Rev. 2017 Jan 13;1:CD010369. PubMed: PM28084646

35. Bright RJ, Wilkinson J, Coventry BJ. Therapeutic options for chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review. BMC Neurol [Internet]. 2014 Feb 7 [cited 2017 Oct 26];14:26. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3925253 PubMed: PM24507546

36. Liu J, Wang LN, McNicol ED. Pharmacological treatment for pain in Guillain-Barré syndrome. Cochrane Database of Systematic Reviews [Internet]. 2015 [cited 2017 Oct 26];4:CD009950. Available from : http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009950.pub3/full

37. Eftimov F, Winer JB, Vermeulen M, de Haan R, van Schaik I. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. Cochrane Database Syst Rev. 2013 Dec 30;(12):CD001797. PubMed: PM24379104

Randomized Controlled Trials – Approved Indications

38. Markvardsen LH, Sindrup SH, Christiansen I, Olsen NK, Jakobsen J, Andersen H, et al. Subcutaneous immunoglobulin as first-line therapy in treatment-naive patients with chronic inflammatory demyelinating polyneuropathy: randomized controlled trial study. Eur J Neurol. 2017 Feb;24(2):412-8. PubMed: PM28000311

39. Nobile-Orazio E, Cocito D, Jann S, Uncini A, Beghi E, Messina P, et al. Intravenous immunoglobulin versus intravenous methylprednisolone for chronic inflammatory demyelinating polyradiculoneuropathy: a randomised controlled trial. Lancet Neurol. 2012 Jun;11(6):493-502. PubMed: PM22578914

40. Ye Y, Li SL, Li YJ. Comparison on therapeutic effect of plasma exchange and intravenous immunoglobulin for Guillian-Barre syndrome. Transfus Med. 2015 Apr;25(2):79-84. PubMed: PM25515056

Non-Randomized Studies – Approved Indications

41. Charra B, Hachimi A, Benslama A, Motaouakkil S. Intravenous immunoglobulin vs plasma exchange in treatment of mechanically ventilated adults with Guillain-Barre syndrome. Pan Afr Med J [Internet]. 2014 [cited 2017 Oct 26];18:35. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4215378 PubMed: PM25368724

42. Markvardsen LH, Harbo T, Sindrup SH, Christiansen I, Andersen H, Jakobsen J, et al. Subcutaneous immunoglobulin preserves muscle strength in chronic inflammatory demyelinating polyneuropathy. Eur J Neurol. 2014 Dec;21(12):1465-70. PubMed: PM25041191

Review Articles

43. Dhawan PS, Goodman BP, Harper CM, Bosch PE, Hoffman-Snyder CR, Wellik KE, et al. IVIG versus PLEX in the treatment of worsening myasthenia gravis: what is the evidence?: a critically appraised topic. Neurologist. 2015 May;19(5):145-8. PubMed: PM25970838

44. Patwa HS, Chaudhry V, Katzberg H, Rae-Grant AD, So YT. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012 Mar 27;78(13):1009-15. PubMed: PM224542686