Acute Treatment of Migraine in Children aged 6-11: Real-World Analysis of Remote Electrical Neuromodulation (REN)

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BACKGROUND

Migraine is a prevalent neurological disorder severely impacting children and adolescents, yet only one pharmacological treatment is approved for ages 6-12 years. Remote Electrical Neuromodulation (REN) is nonpharmacological, prescribed, wearable-device, FDAcleared for acute and/or preventive treatment of migraine with or without aura in patients 12 years and older. This study evaluates REN's safety and efficacy in 6-11 years old.



METHODS

Prospective acute treatment of migraine data was collected through the REN device (Nerivio[®]) smartphone application. Endpoints were device safety (primary); consistent treatment efficacy (headache pain, functional disability, associated migraine symptoms) and REN-medication combinations 2-hours post-treatment.

REFERENCES

1. Abu-Arafeh I, Razak S, Sivaraman B, Graham C. Prevalence, disease burden, and the need for preventive therapy. 1990 to 2019. The Journal of Headache and Pain. 2023 Jul 27;24(1):94. 3. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF, et al. Migraine prevalence, disease burden, and the need for preventive therapy. P. 2. Yang Y, Cao Y. Rising trends in the burden of migraine prevalence, disease burden, and the need for preventive therapy. 1990 to 2019. The Journal of Headache and Pain. 2023 Jul 27;24(1):94. 3. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007 Jan 30;68(5):343–9. 4. Abu-Arafeh I, Howells R. Primary headache and migraine prevalence, disease burden, and the need for prevalence, disease burden, and the need for prevalence of headache and point and the need for prevalence, disease burden, and the need for prevalence, disease burden, and the need for prevalence of headache and point and the need for prevalence, disease burden of migraine and tension-type headache and point and the need for prevalence, disease burden of migraine prevalence, disease burden, and the need for prevalence, disease burden of migraine p age of 7 years. Curr Pain Headache Rep. 2014 Mar;18(3):401. 5. Gelfand AA, Reider AC, Goadsby PJ. Cranial autonomic symptoms in pediatric Migraines. Continuum (Minneap Minn). 2021 Jun 1;27(3):431-6. 6. Hershey AD, Quality of life in childhood migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraine. Headache in Childhood migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, Lewis D, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact and comparison to other N, et al. Use of the ICHD-II Criteria in the Diagnosis of Pediatric Migraines: clinical impact 11. O'Donnell DM, Agin A. Management of headaches: The Journal of Head and Face Pain. 1993;33(1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: nethidren and adolescents. Current Problems in children with disability for 328 (1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: The Journal of Head and Face Pain. 1993;33(1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: The Journal of Head and Face Pain. 1993;33(1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: nethidren and adolescents. Current Problems in children and Face Pain. 1993;33(1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: nethidren and adolescents. Current Problems in children with disability for 328 (1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: Nethidren and adolescents. Current Problems in children and rational incidence, and years lived with disability for 328 (1):29–35. 11. O'Donnell DM, Agin A. Mahagement of headaches: Nethidren and adolescents. Current Problems in children and curre 12. Vos T, Lim SS, Abbasi M, Abbasi M, Saarinen MM. Long term outcome of Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–66. 15. Furnham A, Cheng H. Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–66. 15. Furnham A, Cheng H. Childhood onset of migraine, gender, psychological distress and injuries for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct 17;390(10100):1211–59. 13. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi For the Global Burden of Disease Study 2019. The Lancet. 2020 Oct 17;390(10258):1204–22. 14. Sillanpää M, Saarinen MM. Long term outcome of Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–66. 15. Furnham A, Cheng H. Childhood onset for the Global Burden of Disease Study 2019. The Lancet. 2017;390(10100):1211–59. 13. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Saarinen MM. Long term outcome of Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–66. 15. Furnham A, Cheng H. Childhood onset of migraine, gender, psychological distress and injuries for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct 17;390(10100):1211–59. 13. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Saarinen MM. Long term outcome of childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–66. 15. Furnham A, Cheng term outcome of Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–60. 15. Furnham A, Cheng term outcome of Childhood onset headache: A prospective community study. Cephalalgia. 2018 May;38(6):1159–60. 15. Furnham A, Cheng term outcome of Childhood onset headache: A prospective community study. Cephalagia. 2018 May;38(6):1159–60. 15. Furnham A, Cheng term outcome of Childhood onset headache: A prospective community study. Cephalagia. 2018 May;38(6):1159–60. 15. Furnham A, Cheng term outcome of Childhood onset headache: A prospective community study. Cephalagia. locus of control as predictors of migraine in adulthood. Psychol Health Med. 2023;28(8):2045–57. 16. Kroon Van Diest AM, Ernst MM, Slater S, Powers SW. Similarities and Differences Between Migraine in adulthood. Psychol Health Med. 2023;28(8):2045–57. 16. Kroon Van Diest AM, Ernst MM, Slater S, Powers SW. Similarities and Differences Between Migraine in children and adolescents: Report of the American Headache Rep. 2017 Oct 25;21(12):48. 17. Oskoui M, Pringsheim T, Holler-Managan Y, Potrebic S, Billinghurst L, Gloss D, et al. Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Update summary: Acute treatment of migraine in children and adolescents: Report of the American Headache Rep. 2017 Oct 25;21(12):48. 17. Oskoui M, Pringsheim T, Holler-Managan Y, Potrebic S, Billinghurst L, Gloss D, et al. Practice guideline Update summary: Acute treatment of migraine in children and adolescents: Report of the American Headache Rep. 2017 Oct 25;21(12):48. 17. Oskoui M, Pringsheim T, Holler-Managan Y, Potrebic S, Billinghurst L, Gloss D, et al. Practice guideline Update summary: Acute treatment of migraine in children and adolescents: Report of the American Headache Rep. 2017 Oct 25;21(12):48. 17. Oskoui M, Pringsheim T, Holler-Managan Y, Potrebic S, Billinghurst L, Gloss D, et al. Practice guideline Update summary: Acute treatment of migraine in children and adolescents: Report of the American Headache Rep. 2017 Oct 25;21(12):48. 17. Oskoui M, Pringsheim T, Holler-Managan Y, Potrebic S, Billinghurst L, Gloss D, et al. Practice guideline Update summary: Acute treatment O, Billinghurst L, Gloss D, et al. Practice guideline Update summary: Acute treatment O, Billinghurst L, Billi Society. Neurology. 2014 Sep 10;93(11):487–99. 18. Gelfand AA. Predictors of Triptan Response in Pediatric Migraine. The Lancet Neurology. 2010 Mar 1;9(3):285–98. 21. Diener HC, Limmroth V. Medication-overuse of acute migraine. The Lancet Neurology. 2010 Mar 1;9(3):285–98. 21. Diener HC, Limmroth V. Medication overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2010 Mar 1;9(3):285–98. 21. Diener HC, Limmroth V. Medication-overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–83. 22. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–40. 20. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–40. 20. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–40. 20. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–40. 20. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 Aug 1;3(8):475–40. 20. Bigal ME, Lipton RB. Overuse of acute migraine. The Lancet Neurology. 2014 A migraine chronification. Current opinion in supportive and preventive treatment of episodic or chronic Migraine in patients 12 years and older. Expert Rev Med Devices. 2015;9(2):131-7. 23. Nir RR, Yarnitsky D. Conditioned pain modulation. Current opinion in supportive and preventive treatment of episodic or chronic Migraine in patients 12 years and older. Expert Rev Med Devices. 2015;9(2):131-7. 24. Babaei M, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote Electrical Anal Stud. 2016 Aug;(39):1-46. 26. Yarnitsky D, Edua Stud Neuromodulation (REN) Relieves Acute Migraine: A Randomized, Double-Blind, Placebo-Controlled, Placebo-Controlled, Placebo-Controlled, Nulticenter Trial. Headache: The Journal of Head and Face Pain. 2019;59(8):1240-52. 27. Yarnitsky D, Volokh L, Ironi A, Weller B, Shor M, Shifrin A, et al. Remote electrical stimulation alleviates episodic migraine prevention: A double-blind, randomized, placebo-controlled clinical trial. Headache: 2023 Mar;63(3):377-89. 29. Hershey AD, Lin T, Gruper Y, Harris D, Ironi A, Berk T, et al. Remote . 31. Honteith TS, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Shmuely S, Harris D, Garas S, Ironi A, et al. Remote electrical neuromodulation (REN). Pediatric Neurology. 2023 May 1;142:51–5. 31. Monteith TS, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Ironi A, et al. Remote electrical neuromodulation (REN). Pediatric Neurology. 2023 May 1;142:51–5. 31. Monteith TS, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Stark-Inbar A, Ironi A, et al. Remote electrical neuromodulation (REN). Pediatric Neurology. 2023 May 1;142:51–5. 31. Monteith TS, Stark-Inbar A, Ironi A, et al. Remote electrical neuromodulation (REN). Pediatric Neurology. 2023 May 1;142:51–5. 31. Monteith TS, Stark-Inbar A, Sta Y, Ironi A, Harris D, et al. Comparison of Remote Electrical Neuromodulation for acute treatment of Chronic A, Balani J, Rabany L, Tamir S, Ironi A, Starling A. Real-World Analysis of Remote Electrical Neuromodulation for acute treatment of Chronic A, Balani J, Rabany L, Tamir S, Ironi A, Starling A. Real-World Analysis of Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Manag. 2022 Apr;12(3):267–81. 34. Ailani J, Rabany L, Tamir S, Ironi A, Starling A. Real-World Experience with Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience with Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Analysis of Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience with Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience with Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience With Remote Electrical Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience Neuromodulation for acute treatment of Chronic migraine. Pain Res (Lausanne). 2021;2:753736. 35. Tepper SJ, Lin T, Montal T, Ironi A, Starling A. Real-World Experience Neuromodulation for acute treatment of Chronic migraine. Neuromodulation in the Acute Treatment of Remote Electrical Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, Hämäläinen ML, Eerola M, Hoppu K. A randomized trial of rizatriptan in pediatric migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, Hämäläinen ML, Eerola M, Hoppu K. A randomized trial of rizatriptan in migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, Hämäläinen ML, Eerola M, Hoppu K. A randomized trial of rizatriptan in migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, Hämäläinen ML, Eerola M, Hoppu K. A randomized trial of rizatriptan in migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, et al. Efficacy and tolerability of rizatriptan in migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, et al. Efficacy and tolerability of rizatriptan in pediatric migraine Treatment of Nigraine. Pain Med. 2020 Dec 25;21(12):3522-9. 38. Ho TW, Pearlman E, Lewis D, et al. Efficacy and tolerability of rizatriptan in pediatric migraine attacks in children. Neurology. 2006 Oct 10;67(7):1135-40. 38. Ho TW, Pearlman E, Lewis D, et al. Efficacy and tolerability of rizatriptan in pediatric migraine Treatment. Adv Ther. 2024 Jan;41(1):170-81. 37. A placebo-controlled trial using a novel adaptive enrichment design. Cephalalgia. 2012 Jul;32(10):750-65. 39. Kacperski J, Hershey AD. Newly Approved Agents for the Treatment and Prevant WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of heat and pressure pain. Pain. 2005 Jun;115(3):410-8. 41. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine. CNS Drugs. 2016 Sep;30(9):837-44. 40. Lautenbacher S, Kunz M, Strate P, Nielsen J, Arendt-Nielsen J, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine. CNS Drugs. 2016 Sep;30(9):837-44. 40. Lautenbacher S, Kunz M, Strate P, Nielsen J, Arendt-Nielsen J, Arendt 44. Orenius T, LicPsych null, Sailä H, Mikola K, Restew and Network Meta-analysis. JAMA Pediatric Migraine Prophylaxis: A Systematic Review of Psychologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 12;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 2;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, Berde CB, et al. Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine. N Engl J Med. 2017 Jan 2;376(2):115–24. 43. Locher C, Kossowsky J, Koechlin H, Lam TL, Barthel J, B Behavioral, and Contextual Factors. SAGE Open Nurs. 2018;4:2377960818759442. 45. Taddio A, Ipp M, Thivakaran S, Jamal A, Parikh C, Smart S, et al. Survey of the prevalence of immunization non-compliance due to needle fears in children and adults. Vaccine. 2012 Jul 6;30(32):4807–12.





Efficacy in at least 50% of REN treatments was calculated from all patients who voluntarily reported pain levels, symptoms, and/or disability at treatment-onset and at 2-hours posttreatment, with 72.2% (13/18) patients reporting pain relief, 36.0% (9/25) pain freedom, 83.3% (15/18) functional disability relief, 38.9% (7/18) functional disability freedom.

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one associated symptom.

RESULTS

Children (n=293), median age 11 (IQR=9-11), 73.7% girls, conducted 5,493 REN treatments.

No adverse events and no device-related adverse events were reported. An additional analysis assessed the number of device-related customer support inquiries conducted by this patient cohort (usually through their parents), showing an average of 0.072 inquiries per child, which is similar to the inquiry rate of the entire population of REN users, in all ages (0.067)

> treatment of migraine for children. Providers and families seeking a safe, effective, pill- and needle-free treatment option for children suffering from migraine may consider REN.









