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England

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Clinical management of acute flaccid paralysis / acute flaccid myelitis (AFP/AFM)

Information for health professionals

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Published June 2019

PHE publications

gateway number: 2018715

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Background

Public Health England has received an increase in reports of acute flaccid paralysis and acute flaccid myelitis (AFP/AFM) cases in England, particularly since September 2018. In response, PHE has declared a national incident with the aim of strengthening current surveillance for AFP/AFM and to gather more information on clinical history, possible risk factors and outcomes for cases reported in 2018.

Cases are defined as:

Acute flaccid paralysis/myelitis in an individual aged 30 years and under, not explained by a non-infectious cause.

This guidance summarises existing evidence for the management of AFP/AFM based on US Centers for Disease Control and Prevention (CDC) guidance (1), a recent review of management considerations (2), and an updated Medline literature review.

Infection control procedures are outlined in Appendix 1.

Supportive care

Supportive care is the mainstay of acute treatment of a case of AFP/AFM. The priority for the immediate management is to ensure that the patient's airway is secure. High dependency or intensive care unit admission should be considered according to neurological progression or deficits present; mechanical ventilation is required in up to 20% of patients (2, 3).

Immunological therapies

Intravenous immunoglobulin (IVIg)

IVIg is generally safe and well tolerated. Possible adverse effects include fever, headache, myalgia, chills, nausea, and vomiting, anaphylactoid symptoms (flushing, tachycardia, and hypotension), aseptic meningitis, fatigue, and arthralgia. Rarely, severe adverse events have been reported including acute renal failure, thromboembolic events, haemolytic anaemia, and neutropenia (1).

The efficacy of intravenous immunoglobulin (IVIG) to treat AFP/AFM has not been systematically studied, with data limited to case reports or case series (1). In agammaglobulinaemic children, enteroviral infection has been associated with severe neurological disease, suggesting that antibody helps prevent severe disease (4). IVIG preparations have been shown to contain antibody against circulating enteroviruses (EV), including EV-D68 (5). In rodents, IVIG has been found to have some efficacy in preventing progression to neuroinvasive disease (1). In order to be effective, IVIG administration as early as possible after onset of symptoms is likely required. Intramuscular immunoglobulin administration to susceptible populations in outbreak situations has shown some efficacy in preventing poliomyelitis (6). A randomised control trial to treat pre-paralytic poliomyelitis with intramuscular immunoglobulin, however, showed no efficacy in preventing progression to paralytic disease or reducing disease severity(7),

IVIG is currently in very short supply, especially in the UK. Acute disseminated encephalomyelitis (if high-dose steroids have failed) is a grey indication for IVIG. Grey indications are those for which evidence is weak, primarily because the disease is rare, and requires local approval (8).

Corticosteroids

There is no clear evidence that steroids are beneficial or harmful in the treatment of AFP. Steroids are indicated for acute cord swelling and for conditions that may be included in the differential diagnosis for AFP, including transverse myelitis and acute disseminated encephalomyelitis. Nevertheless, steroids could impair the immune response to AFP due to an infectious cause. Steroid use has been associated with poorer outcome in outbreaks of enterovirus A71 (EV-A71) and in mouse models of acute flaccid myelitis with enterovirus D68 (EV-D68) (9, 10). EV-A71 and EV-D68 have both been associated with neurological disease (1).

Plasma exchange

There is no clear evidence that plasma exchange is beneficial or harmful in the treatment of AFP. As noted above, humoral immune response appears to be important in reducing the severity of AFP associated with acute viral infection; therefore removal of antibodies through plasma exchange could cause potential harmful effects. Most case series have reported no clinical improvement or adverse events associated with plasma exchange (1). In a single case report, there was significant improvement following treatment with plasmapheresis, IVIG and corticosteroids (11).

Interferon

There is no indication that interferon is beneficial in the treatment of AFP. Some case series have suggested that interferon-alpha may be associated with improvements in West Nile poliomyelitis-like illness and Saint Louis encephalitis, though others have reported no effect (1). A randomised trial of the use of interferon to treat Japanese encephalitis showed no benefit compared to placebo (12). Interferon could theoretically be harmful due to its immunomodulatory effects.

Antiviral therapies

Fluoxetine

Available data suggest that, while well-tolerated, there is no evidence that fluoxetine is effective at improving neurological outcomes in patients with acute flaccid myelitis. Fluoxetine is a selective serotonin reuptake inhibitor which has shown *in vitro* antiviral activity against EV-D68 (13). A cohort study of US patients with acute flaccid myelitis found that patients treated with fluoxetine administered at a median of 5 (IQR 3-7) days after neurological onset had no improvement in limb strength at follow-up. Fluoxetine was preferentially given to patients with EV-D68 in this study (13). A study in mice with EV-D68 induced paralysis also found that fluoxetine had no effect on paralysis outcomes compared to controls (10).

Other Antivirals

There is no indication that any other antivirals are beneficial in the treatment of AFP unless herpesvirus infection is suspected. The CDC have found no evidence that pleconaril, pocapavir, and vapendavir have any significant activity against EV-D68 (14). If herpesvirus infection is suspected, appropriate antivirals (i.e., acyclovir, valaciclovir) should be empirically administered until herpesvirus infection has been excluded or, if confirmed, appropriately treated (1).

Long-term outcomes

While most reports suggest some improvement, AFP is commonly associated with a persistent neurological deficit. A systematic review found that only 7 of 61 cases with AFP associated with non-polio enteroviruses since 2014 had full recovery (15).

Rehabilitation

Early physiotherapy and occupational therapy to maintain supple passive range of movement in the affected limbs during the period of paralysis is key to treatment. Evidence suggests that children with acute flaccid myelitis and other forms of myelitis can continue to regain strength and function in affected limbs for months to years following presentation (2).

Nerve transfer

Nerve transfers are known to be beneficial in restoring innervation and function to denervated muscles*. Nerve transfer involves the re-routing of parts of functioning nerves from a functioning muscle to reinnervate muscles that are considered more useful. (2). Case reports of patients with AFP report more upper, over lower limb, involvement and proximal muscle involvement over distal; and thus are well suited to the well understood and well utilised tool of nerve transfer surgery (18). Whilst identification of the ideal timing for nerve transfer in this cohort is not clear (16), It is well understood that, in those who will not finally reinnervate, the surgery should be performed as soon as possible for best outcome, and absolutely before 9 to 12 months post onset of paralysis. The identification of patients that will not spontaneously recover is the challenge, and local protocols in the USA are suggesting that any patient who has muscle which has not reinnervated by 3 (and certainly by 6 months) should be considered for nerve transfer surgery (19).

Functional electrical stimulation

Other strategies used in the rehabilitation of children with transverse myelitis, such as functional electrical stimulation (neuroprostheses that stimulate muscles that have lost function via electrical stimulation) may also be considered in order to restore function though their effectiveness in AFP has not been evaluated (17) and in conditions of peripheral axonal degeneration with denervated muscle evidence in clinical studies for electrical stimulation is limited and based on small case series reports (20).

References

1. Centre for Disease Control and Prevention. Acute Flaccid Myelitis: Interim Considerations for Clinical Management 2014 [Available from: <https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinical-management.html>].
2. Hopkins SE. Acute Flaccid Myelitis: Etiologic Challenges, Diagnostic and Management Considerations. Current treatment options in neurology. 2017;19(12):48.
3. Sejvar JJ, Lopez AS, Cortese MM, Leshem E, Pastula DM, Miller L, et al. Acute Flaccid Myelitis in the United States, August-December 2014: Results of Nationwide Surveillance. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2016;63(6):737-45.
4. Wilfert CM, Buckley RH, Mohanakumar T, Griffith JF, Katz SL, Whisnant JK, et al. Persistent and fatal central-nervous-system ECHOvirus infections in patients with agammaglobulinemia. The New England journal of medicine. 1977;296(26):1485-9.
5. Zhang Y, Moore DD, Nix WA, Oberste MS, Weldon WC. Neutralization of Enterovirus D68 isolated from the 2014 US outbreak by commercial intravenous immune globulin products. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2015;69:172-5.
6. Hammon WD, Coriell LL, Ludwig EH, et al. Evaluation of red cross gamma globulin as a prophylactic agent for poliomyelitis: 5. reanalysis of results based on laboratory-confirmed cases. Journal of the American Medical Association. 1954;156(1):21-7.
7. Bahlke AM, Perkins JE. Treatment of preparalytic poliomyelitis with gamma globulin. Journal of the American Medical Association. 1945;129(17):1146-50.
8. Wimperis J, Lunn M, Jones A, Herriot R, Wood P, O'Shaughnessy D, et al. Clinical Guidelines for Immunoglobulin Use, 2nd edn update. Department of Health Publication. 2011.
9. World Health Organisation. Severe complications of hand, foot and mouth disease (HFMD) caused by EV-71 in Cambodia – conclusion of the joint investigation 2012 [Available from: https://www.who.int/csr/don/2012_07_13/en/].
10. Hixon AM, Clarke P, Tyler KL. Evaluating Treatment Efficacy in a Mouse Model of Enterovirus D68-Associated Paralytic Myelitis. The Journal of infectious diseases. 2017;216(10):1245-53.
11. Esposito S, Chidini G, Cinnante C, Napolitano L, Giannini A, Terranova L, et al. Acute flaccid myelitis associated with enterovirus-D68 infection in an otherwise healthy child. Virology journal. 2017;14(1):4-.
12. Solomon T, Dung NM, Wills B, Kneen R, Gainsborough M, Diet TV, et al. Interferon alfa-2a in Japanese encephalitis: a randomised double-blind placebo-controlled trial. Lancet (London, England). 2003;361(9360):821-6.
13. Messacar K, Sillau S, Hopkins SE, Otten C, Wilson-Murphy M, Wong B, et al. Safety, tolerability, and efficacy of fluoxetine as an antiviral for acute flaccid myelitis. Neurology. 2018;10.1212/WNL.0000000000006670.
14. Rhoden E, Zhang M, Nix WA, Oberste MS. In Vitro Efficacy of Antiviral Compounds against Enterovirus D68. Antimicrobial agents and chemotherapy. 2015;59(12):7779-81.
15. Suresh S, Forgie S, Robinson J. Non-polio Enterovirus detection with acute flaccid paralysis: A systematic review. J Med Virol. 2018;90(1):3-7.
16. Isaacs, J. & Cochran, A.R., 2019. Nerve transfers for peripheral nerve injury in the upper limb. *The bone & joint journal*, 101-B(2), pp.124–131.

17. Saltzman EB, Rancy SK, Sneag DB, Feinberg Md JH, Lange DJ, Wolfe SW. Nerve Transfers for Enterovirus D68-Associated Acute Flaccid Myelitis: A Case Series. *Pediatric neurology*. 2018;88:25-30.
18. PN 11. **Markers of Spontaneous Recovery Versus Surgical Intervention In Acute Flaccid Myelitis (AFM)** Erin L Weber, MD, PhD; Mitchel Seruya, MD *University of Southern California, Los Angeles, CA* <http://peripheralnerve.org/meeting/abstracts/2019/PN11.cgi>
19. Peckham PH, Knutson JS. Functional Electrical Stimulation for Neuromuscular Applications. *Annual Review of Biomedical Engineering*. 2005;7(1):327-60.
20. Novak CB, von der Heyde RL. Evidence and techniques in rehabilitation following nerve injuries. *Hand Clin*. 2013;29(3):383–92.

Appendix 1: Infection Control Procedures

There is no common unifying aetiology for AFP/AFM cases. Enteroviral infections are the most prominent infectious causes identified. Enteroviruses, including poliovirus, are transmitted by faecal oral route, respiratory secretions (especially EV-D68) or close contact with infected people. Enteroviruses are non-enveloped RNA viruses and have greater environmental stability than many other viruses. Given this information, PHE currently recommends standard + contact + droplet infection control precautions until the aetiology of each individual case of AFP/AFM has been further identified, because there are many possible causes of AFP/AFM: <https://www.cdc.gov/acute-flaccid-myelitis/hcp/faqs.html>.

As enteroviruses are non-enveloped viruses and, therefore, less susceptible to disinfectants and alcohol based hand rub, strict hand hygiene is of utmost importance. Hands should be decontaminated with **liquid soap and water** as per the WHO “5 Moments of Hand Hygiene”:

- before touching a patient
- before clean/aseptic procedure
- after body fluid exposure risk
- after touching a patient
- after touching patients surroundings.

Alcohol-based hand rub alone should not be used to decontaminate hands.

Bitnun, A. and Yeh, E. A. (2018) ‘Acute Flaccid Paralysis and Enteroviral Infections’, *Current Infectious Disease Reports*. Springer US, 20(9), p. 34. doi: 10.1007/s11908-018-0641-x.

Macesic, N. et al. (2016) ‘Acute Flaccid Paralysis: The New, The Old, and The Preventable’, *Open Forum Infectious Diseases*. Oxford University Press, 3(1), p. ofv190. doi: 10.1093/ofid/ofv190.

Sejvar, J. J. et al. (2010) ‘Clinical assessment of self-reported acute flaccid paralysis in a population-based setting in Guatemala.’, *The American journal of tropical medicine and hygiene*. The American Society of Tropical Medicine and Hygiene, 82(4), pp. 712–6. doi: 10.4269/ajtmh.2010.09-0090.

Solomon, T. and Willison, H. (2003) ‘Infectious causes of acute flaccid paralysis’, *Current Opinion in Infectious Diseases*, 16, pp. 375–381. doi: 10.1097/01.qco.0000092807.64370.1e.