

Selected Summaries

Containment of Measles Outbreak by Active Immunization

[De Serves G, Boulianne N, Ratnam S, Corriveau A. Effectiveness of vaccination at 6 months of age during an outbreak of measles. Pediatrics 1996, 97: 232-235.]

During an outbreak of measles, there are two possible ways to protect susceptible infants; administration of immunoglobulins or vaccinating the child against measles. Immunoglobulins are effective in decreasing the severity of disease soon after administration, but they are not effective in controlling an outbreak of measles. During an outbreak of measles in Canada, monovalent live attenuated measles vaccine was administered to infants aged 6 to 11 months living in the affected communities. Active surveillance was used to detect cases of measles occurring during the following months. The Canadian measles case definition—fever greater than 38.3°C, generalized rash and at least one of the symptoms of cough, coryza or conjunctivitis—was determining cases. All children vaccinated at the age of 6 to 11 months were asked to return at 15 months for revaccination. Children who did not develop measles were tested for measles antibody using plaque reduction neutralization test before revaccination.

Of 81 children 6 to 11 months of age, 56 were vaccinated and two received immunoglobulins; the latter were excluded from the analysis. The overall attack rate of measles during and after vaccination campaign was 19% (15 out of 79 children). The attack rate among unvaccinated children was 39%

(9 of 23), compared with 11% (6 of 56) amongst those vaccinated (relative risk=3.6, 95% confidence interval [CI]=1.5 to 9.1). All those who developed measles in the vaccinated group did so within 10 days after immunization. The overall vaccine effectiveness was 73% (95% CI=32% to 89%) when children were classified as vaccinated as soon as they were given measles vaccine. However, the effectiveness rose to 96% (95% CI=76% to 99%) when children were considered vaccinated a week after their injections, as this is the time generally necessary to induce a response. Nineteen children who were vaccinated and did not develop measles during the outbreak had significant neutralizing antibody titers at 15 months of age even without revaccination. It was concluded that measles vaccination of infants aged 6 to 11 months is an effective intervention measure during measles outbreak.

Comments

The American Academy of Pediatrics recommends that during an outbreak of measles, when the risk of community exposure is high, infants as young as 6 months of age should be administered measles vaccine with revaccination at 15 months of age. However, vaccination at less than 9 months of age remains controversial. Some earlier studies(1-3) indicate that those children who are given the first dose of measles vaccine at 6 to 11 months tend to have lower antibody titers than those who are vaccinated once at 15 months; and that early administration of measles vaccine may produce a cohort of children with inadequate immunity who cannot be fully immunized even by revaccination. This antibody response has, however, not been

found in certain other studies(4). In the present report, the antibody titers of the children at 15 months of age before the administration of second dose of measles vaccine were significant. The distribution of antibody titers was similar for children vaccinated at 6 to 8 months of age and at 9 to 11 months of age.

This study could not have been conducted as a randomized, placebo controlled vaccine efficacy study because of ethical and practical considerations. In the absence of randomization, the risk for exposure to measles should be comparable between vaccinated and unvaccinated children to ensure the validity of vaccine efficacy estimates. This risk was assumed to be the same within the small tight knit community. As most cases of measles amongst those unvaccinated occurred before the initiation of control measures, there is a possibility that infants who were immune enough to resist measles during the initial phase of outbreak were also those who received vaccination. It was also assumed that the distribution of maternally derived antibody titers were similar between vaccinated and unvaccinated children. In spite of

these drawbacks, the present study carried out during an outbreak of measles provides data to support the current recommendation to vaccinate children at 6 to 11 months of age as part of outbreak control strategy.

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REFERENCES

1. Murphy MD, Brunei PA, Lievens AW, Shehab ZM. Effect of early immunization on antibody response to reimmunization with measles vaccine as demonstrated by ELISA. *Pediatrics* 1986, 74: 90-96.
2. Stetler HC, Oreinstein WA, Bernier RH, *et al.* Impact of revaccinating children who initially received measles vaccine before 10 months of age. *Pediatrics* 1986, 77: 471-476.
3. Black FL, Berman LL, Libel M, *et al.* Inadequate immunity to measles in children vaccinated at an early age; effect of revaccination. *Bull WHO* 1984, 62: 315-319.
4. McGraw TT. Reimmunization following early immunization with measles vaccine. *Pediatrics* 1986, 77: 45-48.

Guillian-Barre Syndrome : Issues in Etiology and Management

[Korinthenberg R, Schulte Monting J. Natural history and treatment effects in Guillian-Barre syndrome: A multicenter study. Arch Dis Child 1996, 74:281-287.]

Guillian-Barre syndrome is a leading cause of acute paralysis in children. In general the clinical findings, progression and

outcome have been similar in children and adults, but management of pediatric Guillian-Barre syndrome is subtly different. This multicentre retrospective study was performed to investigate the natural course and treatment effects in pediatric Guillian-Barre syndrome. Authors sent structured questionnaire to 155 pediatric hospitals of Germany and Switzerland and asked for details of patients who strictly fulfilled the diagnostic criteria of Guillian-Barre syndrome. The questionnaire was designed to include details of preceding ill-

ness, progressive phase, paraclinical findings (cerebrospinal fluid and electrophysiology), treatment modality, and recovery. The degree of disability was coded in 10 levels. These functional levels were defined in a way that could be expected to produce reliable data in a retrospective study. Progression rate was calculated dividing maximum disability by duration of progression. Authors thus, presented analysis of 175 patients. The age of patients ranged from 11 months to 17.7 years. There was slight preponderance of boys. In approximately 79% of patients, a preceding illness was reported. Upper respiratory tract infections were most common, followed by gastrointestinal infections. In few patients, specific infective agents could be identified by different serological tests. *Campylobacter jejuni* was detected in two cases.

At the peak stage of the disease, 26% of the patients were ambulatory. The median time from onset of symptoms to first recovery was 17 days, to walk unaided 37 days, and to be free of symptoms 66 days. At long term follow up, 98 out of 106 patients were free of symptoms and remainder were able to walk unaided. Approximately 16% of children had been artificially ventilated. Maximum disability score was the most powerful prognostic factor. Axonal nerve conduction changes were indicative of a longer duration of total illness. Axonal changes were present in 19% of patients, all were of older age group.

Corticosteroids (n=33), intravenous immunoglobulins (n=70) and plasmapheresis (n=19), were treatment modalities that had been used depending on the age of the patient and severity of disease. Plasmapheresis was performed in older patients with a very high disability. The group without any treatment consisted of young children with low severity. Immunoglobulins were shown to accelerate re-

covery while Corticosteroids were less effective. Plasmapheresis could not be evaluated because it was administered only in most severe cases. Authors concluded that the natural history of Guillian-Barre syndrome in children is extremely variable and more benign than in adults. Treatment with immunoglobulins should be considered in patients unable to walk. Corticosteroids are not as effective and should be withheld except when the disease has a prolonged course.

Comments

In Guillian-Barre syndrome there is an immune-mediated attack on the myelin sheath of peripheral nerves. It is also known as acute inflammatory demyelinating polyneuropathy (AIDP). In Guillian-Barre syndrome severe inflammation may induce secondary axonal degeneration - a "bystander" effect. Recovery in these cases is more prolonged(1). Although *Campylobacter* infection is common in children, only a few reports of Guillian-Barre syndrome following this infection are available(2). Most often, a non-specific upper respiratory infection has occurred within 4 weeks before neurological symptoms, as has been seen in this study. In the Chinese patients, clinical, electrophysiological and pathological studies(3) revealed an 'acute motor axonal neuropathy' in children and young adults which was similar to Guillian-Barre syndrome. However, there was also a primary axonal degeneration that affected only motor fibres. These cases tend to occur in summer and had been linked to infection with *Campylobacter jejuni* which in adults is now regarded as the chief precipitant of Guillian-Barre syndrome(4). In this study, only two cases were linked to *Campylobacter* infection. Older patients with the more severe and axonal form are more likely to have *Campylobacter jejuni* infection. It has been

observed that *Campylobacter jejuni* positive patients more often required ventilatory support and became bed bound within two days of neurological symptoms, the median time to regain ability to walk was 89 days as compared with 45 days for *Campylobacter jejuni* negative patients(5) Possibly, the lack of frequent *Campylobacter jejuni* infections, is responsible for the more benign nature of illness in children

At present, the management of Guillian Barre syndrome in children is similar to that in adults In children, treatment with corticosteroids, plasmapheresis and intravenous immunoglobulins have not been adequately assessed so far(2) In adults, plasmapheresis is indicated in cases of severe progressive disease and should be given early in the illness It is not indicated for patients with only mild disease and for those in whom the disease is no longer progressing^ It can not be used in small children due to technical difficulties There is no evidence to support the use of corticosteroids for the treatment of this disease A recent multicenter British study(6) found no benefit from administration of high dose methyl-prednisolone early in the course of the disease A Dutch multicentric controlled study(7) of intravenous human immunoglobulins was found to be atleast as effective as plasmapheresis(8)

It could be started immediately avoiding delays in transferring patients to specialized centers for plasmapheresis An other advantage is that some contraindications to plasmapheresis do not apply for treatment with intravenous immunoglobulins In this study also, the authors found that immunoglobulins were able to accelerate the recovery in patients who were unable to walk Both plasmapheresis and highly expensive immunoglobulins are not available to most of patients in this country, where the only option left is corticosteroids

were less effective than immunoglobulins; these accelerated recovery in the early phase but did not have any effect on the final outcome. In patients with protracted course where suspicion of chronic demyelinating polyneuropathy arises, corticosteroids are helpful So, we have to rely on proper general management and prevention of complications The chief complications are respiratory failure and vascular collapse Intubation with an endotracheal tube should be done before the patient complains of air hunger, and assisted respiration should be begun at the first sign of dyspnea or if blood oxygen saturation begins to decrease Sudden precipitous falls in blood pressure may also occur These usually respond best to volume replacement Secondary pressure palsies seems to account for some residual weakness in children and deserve proper attention

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REFERENCES

- 1 Bolton CF The changing concepts of Guillain-Barre Syndrome N Engl J Med 1995;333 1415-1416
- 2 Ropper AH, Wijdicks EFM, Truax BT Guillain-Barre syndrome In Contemporary Neurology Series, Vol 34 Ed Plum F Philadelphia, FA Davis, 1991, pp 122 - 127
- 3 McKhann GM, Cornblath DR, Griffin JW, et al Acute motor axonal neuropathy A frequent cause of acute flaccid paralysis in China Ann Neurol 1993, 33 333-342
- 4 Ho TW, Mishu B, Li CY, et al Guillain-Barre syndrome in Northern China Relationship to *Campylobacter jejuni* infection and antiglycolipid antibodies Brain 1995, 118 597-605
- 5 Rees JH, Soudain SE, Gregson NA,

- Hughes RAC *Campylobacter jejuni* infection and Guillain-Barre syndrome N Engl J Med 1995; 333: 1374-1379.
- 6 Guilhan-Barre Syndiome Steroid Trial Group Double blind trial of intravenous methyl-predmsolone in Guillan-Barre syndrome Lancet 1993; 341: 586-590.
 - 7 Van der Meche FGA, Schmitz PIM, and the Dutch Guilhan Barre study group A randomized trial comparing intravenous immune globulin and plasma exchange in Guilhan Barre syndrome N Engl J Med 1992;326: 1123-1129.
 - 8 Vallee L, Dulac O, Nuys JP, Leclerc F, Vamecq J Intravenous immunoglobulin is also an efficient therapy of acute Guilhan-Barre syndrome in affected children Neuropediatrics 1993; 20: 235-236.

Current Status of Newer Antiepileptic Drugs

[Dichter MA, Brodie MJ *New antiepileptic drug; New Eng J Med 1996 334 1583-1590*]

Epilepsy is a common disorder, often requiring treatment for many years. In a substantial proportion of patients, effective control over seizures is not achieved despite optimal therapy with the established antiepileptic drugs. In some patients the occurrence of side effects warrant discontinuation of the drug. Hence research continues to discover a safe new drug with broad activity and without any side effects which might cure epilepsy.

Three new antiepileptic drugs felbamate, lamotrigine and gabapentin have been in use in the United States for the last two years. They have been approved for use in adults who have partial seizures either alone or with secondary generalized seizures. Only felbamate has been approved by the Food and Drug Administration (USA) for use in children with Lennox Gastaut syndrome(1). However, due to frequent occurrence of hepatotoxicity and aplastic anemia, it is only to be used in patients who have seizures re-

fractory to all other medications. Lamotrigine has been widely used in Europe because it is effective in children with idiopathic generalized seizures and does not impair cognition(2). Similarly, gabapentin because of its relative safety, has been tried in children with focal epilepsy. Hence lamotrigine and gabapentin may be approved by FDA for future use in children.

Clobazam, vigabatrin, oxcarbazepine, zonisamide, gabapentin, topiramate, losigamone, remacemide, levetiracetam and fosphenytoin are currently under trial in the USA. Among these, clobazam (1,5 benzodiazepine) appears to be effective in atonic seizure, typical absence, atypical absence, myoclonic and secondary generalized tonic clonic seizure and in children with Lennox Gastaut Syndrome. Vigabatrin has been found effective in infantile spasms and other uncontrollable seizures in children with neurologic dysfunction. Oxcarbazepine, a 10 ketoanalogue of carbamazepine, has fewer side effects than the parent drug because of metabolism via a different pathway. Zonisamide appears to have a spectrum of activity like carbamazepine. Tiagabine and topiramate are effective for focal seizures. Fosphenytoin which is a water soluble

phenytoin prodrug can be given intramuscularly and is less irritating than the parent drug.

Comments

The search for an ideal antiepileptic drug continues. The efficacy of a new drug can be established only if a reduction in seizures can be demonstrated in patients with uncontrolled seizures despite optimal doses of standard antiepileptic drugs. When used on such patients, these new drugs have shown a 25 to 50% reduction in seizure frequency in about 50% of cases. Once these drugs get approved for use, they may be tried in patients with less severe epilepsy, including those who are being treated for the first time. How effective these drugs will be when used in this way is difficult to predict and will need further trials. All the new drugs have limited efficacy and potential for serious side effects. In developing countries like ours, besides efficacy, cost and ease of availability, are other important factors which determine the use of a

drug. The high cost of these new drugs may be an important limiting factor in their widespread use. Considering all these factors, gabapentin because of its lack of side effects, absence of interaction with other drugs, and good efficacy, is a potential candidate for the first line drug for focal epilepsy in the future. Till further data are available, these newer antiepileptic drugs are likely to be used only if the established drugs fail to control seizures.

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REFERENCES

1. Leppik IE, Dreifuss FE, Pledger GW, *et al.* Felbamate for partial seizures: Results of a controlled clinical trial. *Neurology* 1991; 41:1785-1789.
2. Goa KL, Ross SR, Chrisp P. Lamotrigine: A review of its pharmacological properties and clinical efficacy in epilepsy. *Drugs* 1993; 46:152-176.