

Should children with inherited metabolic disorders receive varicella vaccination?

M Varghese,¹ M Cafferkey,² M O'Regan,¹ A A Monavari,¹ E P Treacy¹

¹National Centre for Inherited Metabolic Disorders, and
²Department of Clinical Microbiology, Children's University Hospital, Temple Street, Dublin, Ireland

Correspondence to

Professor E P Treacy, National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple Street, Dublin 1, Ireland; eileen.treacy@cuh.ie

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ABSTRACT

The aim was to determine the rate of varicella infection and complications in children with disorders of intermediary metabolism (IEM) between the ages of 1 and 16 years attending our national metabolic referral centre. Of 126 children identified, a response was received from 122. A history of previous varicella infection was identified in 64 cases (53%) and of varicella vaccination in 5 (4%). Fifty-three (43%) patients apparently did not have a history of clinical varicella infection. Of the 64 children with a history of varicella infection, five required hospitalisation for complications, including life-threatening lactic acidosis in one patient with mitochondrial disease and metabolic decompensation in four patients. In conclusion, varicella infection may cause an increased risk of metabolic decompensation in patients with IEMs. We propose that a trial of varicella vaccination be considered for this cohort of patients with monitoring of its safety and efficacy.

Communicable infectious diseases of childhood place children with inborn errors of metabolism (IEMs) at high risk of metabolic decompensation with potentially catastrophic consequences. A number of IEMs also have an associated immunodeficiency.¹ Varicella is an acute, highly communicable viral disease with worldwide distribution for which a preventive vaccination is available. In the USA, more than 90% of infections and two thirds of varicella-related hospitalisations and almost half of varicella-related deaths occur in children.² Infection may also be fatal in immunocompromised individuals. Complications include secondary bacterial infections commonly by *Streptococcus pyogenes* and/or *Staphylococcus aureus*.² Other complications include postinfectious cerebellar ataxia, encephalitis and respiratory complications, including pneumonitis.

Varicella vaccine is a live attenuated OKA strain and has been marketed since 1974, with two products now available, the univalent Varicella Virus Vaccine Live (VARIVAX) and multivalent ProQuad (MMR + varicella).³ Varicella vaccine is considered to be 85–90% effective in preventing varicella infection and 100% effective in preventing moderate or severe disease.² Seroconversion after a single dose can reach up to 95% in healthy children. The US Advisory Committee on Immunization Practices (2006) now recommends two doses, the first at 12–15 months and the second at 4–6 years.³

We sought to determine the rate of varicella infection and complications in the cohort of patients with IEMs actively followed at

our centre, the National Centre for Inherited Metabolic Diseases.

METHODS

Patients with inborn errors of intermediary metabolism aged between 1 and 16 years on 1 July 2007 were identified from the National Centre for Inherited Metabolic Disorders database. Patients with Phenylketonuria, Galactosaemia, Homocystinuria and other conditions not associated with major metabolic decompensation during an acute illness were excluded from this study. A questionnaire was mailed to parents to ascertain whether the child had a prior history of varicella infection, any complications following varicella and/or history of varicella vaccination prior to the study.

RESULTS

We identified 126 patients at risk for metabolic decompensation, to whom the questionnaire was mailed. Non-responders were contacted by telephone. The total response rate was 97% (52% by post and 45% by phone). There was a history of varicella in 64 (53%) patients. Five patients had previously been vaccinated. Fifty-three (43%) patients did not have a history of clinical varicella infection. Of a subset of patients⁴ who had varicella serology recently performed and who were deemed from the history not to have been infected, three were found to be positive for varicella antibody. The characteristics of the study cohort and complications documented are described in table 1. Five children were hospitalised with varicella; all had metabolic decompensation on admission and needed intensive treatment. One child who had life-threatening lactic acidosis required intensive care. In addition, four patients with mitochondrial disease developed secondary bacterial skin infections. All skin infections were treated by family doctors, and hospitalisation was not required.

DISCUSSION

Our results indicate that the hospitalisation rate observed following varicella in patients with IEMs was at least 5% in the total group potentially exposed to varicella (7.8% in the respondent group), which is much higher than the complication rate of 0.01% reported in apparently healthy children.^{5 6}

Even allowing for the fact that some children whose families reported no history of varicella may have had subclinical or mild varicella, this hospitalisation rate is still significantly higher

Table 1 Complications of varicella in children with inborn errors of metabolism

Inborn errors of metabolism	Number	History of clinical varicella	Metabolic decompensation needing hospital admission	Secondary bacterial infection
Mitochondrial respiratory chain defect	53	29	2*	5
Fatty acid oxidation disorder	13	10		
Glycogen storage disorder	9	2	1	
Urea cycle disorder	9	6		
Glutaric aciduria	8	5	1	
Mucopolysaccharidosis	7	3		
Maple syrup urine disease	6	0		
Methylmalonic aciduria	5	3	1	
Others	12	6		

*One child admitted to intensive care with lactic acidosis.

than for normal healthy children. The rate of bacterial skin infections observed in the cohort was similar to that for normal healthy children.⁴ There is little data on the complications of varicella in children with IEM. Hospitalisation from varicella in our patients with IEMs was all due to metabolic decompensation, not secondary bacterial infection (in contrast to other children).^{5,6}

Management of our patients typically included administration of “unwell dietary regimens”.

We propose that varicella vaccination in children with IEMs shown by serology to be varicella negative may be beneficial. Follow-up with monitoring of patient seroconversion rates and documentation of any adverse events following vaccination will be required. Potential drawbacks from giving varicella vaccine to children with IEMs are metabolic decompensation and contraindication due to immunodeficiency. Fifteen per cent of children develop a fever following varicella vaccination,^{2,3} so they might be at risk of metabolic decompensation. However, our practice is to give an “unwell regime” with extra calories (or decreased protein intake in the case of organic acidurias) prophylactically at the time of vaccination and as required if there is a fever following vaccination.

Vaccination with varicella vaccine, a live vaccine, may be contraindicated in metabolic diseases associated with a significant

immunodeficiency such as Glycogen Storage Disorder 1b and poorly controlled propionic and methylmalonic aciduria; each case should be evaluated individually.¹

In conclusion, varicella infection may cause an increased risk of metabolic decompensation in patients with IEMs. We propose that a trial of varicella vaccination is considered for this cohort of patients with monitoring of its safety and efficacy.

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Competing interests None.

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