Editorial

Subacute sclerosing panencephalitis: promising results with intraventricular interferon alpha 2b therapy and intraventricular ribavarin therapy

Aulakh R[1]

[1]Dr. Roosy Aulakh, Associate Professor, Department of Pediatrics, Govt. Medical College & Hospital, Sector 32, Chandigarh, India.

Corresponding Author: Dr. Roosy Aulakh, Associate Professor, Department of Pediatrics, Govt. Medical College & Hospital, Sector 32, Chandigarh, India. Email: drroosy@gmail.com

……...

Abstract

Subacute sclerosing panencephalitis (SSPE) is a devastating 'slow virus' disease of childhood and adolescence caused due to persistence of defective measles virus (MV) within the neurons and glial cells. Three drugs, i.e., inosiplex, ribavirin and interferon-alpha (IFN-alpha) were reported to be effective though none of them have been proven to be curative.

Key words: Subacute sclerosing panencephalitis, Inosiplex, Ribavirin, Interferon-alpha (IFN-alpha)

……...

Introduction

Subacute sclerosing panencephalitis (SSPE) is a devastating 'slow virus' disease of childhood and adolescence caused due to persistence of defective measles virus (MV) within the neurons and glial cells. Hyperfusogenic viruses with mutations, unlike the wild-type MV, can induce cell-cell fusion even in SLAM and nectin 4-negative cells and spread efficiently in human primary neurons and the brains of animal models resulting in persistence of defective measles virus manifesting as SSPE later on. The age at presentation is usually 8 to 10 years with latent period of 2-10 years after measles infection. However, SSPE has been previously reported by us in a 2-and-half-year-old boy who presented with progressively increasing myoclonic jerks and subtle cognitive decline and changing epidemiological trends were highlighted [1].

Sahaet al had reported an annual incidence of 21 per million population in India [2] Despite vast coverage with measles vaccination campaign by Government of India, measles has still not been eliminated till date.

SSPE treatment is still of relevance to developing country like India, especially with SSPE incidence of 6.5 to 11 cases per 100000 acute measles infections translating into a SSPE risk of 1 in 9100 to 15400 cases of measles been from the USA, asa much higher incidence is expected in India [3].

Out of several compounds which had been tried for the treatment of SSPE, three drugs, i.e., inosiplex, ribavirin and interferon-alpha (IFN-alpha) were reported to be effective though none of them have been proven to be curative. Further, studies on combination therapy like intraventricular IFN-alpha and ribavirin also reported poor outcomes due to the late onset and rapidly progressing symptoms of the disease [4] Similar observations were put forth by Hara S et al as well [5].

Ribavirin is a broad-spectrum antiviral drug with inhibitory activity against many RNA viruses, including measles virus. Hosoya M et al observed and reported clinical effectiveness (significant neurologic improvement and/or a significant decrease in titers of hemagglutination inhibition antibodies against measles virus in CSF) in four of five patients in whom CSF ribavirin concentrations were maintained at a level at which SSPE virus replication was almost completely inhibited in vitro and in vivo by intraventricular administration [6].

Comparative study of the outcome of pediatric subacute sclerosing pan-encephalitis patients treated with oral ribavirin versus intraventricular interferon alpha 2b via Ommaya reservoir has been reported in current issue by Ghosh KC et al in which intraventricular interferon alpha therapy has been shown to be far superior to oral

ribavirin [7]. Recently Miyazaki K et al reported that the target ribavarin concentration in the cerebrospinal fluid could be maintained continuously by intraventricular administration using a subcutaneous continuous infusion pump without any severe side effect. Furthermore, two out of three patients in whomtreatment was continuing, the patients remain in stage III, while the patient who discontinued the therapy progressed to stage IV [8].

The recent studies, thus, do report promising results in treatment of SSPE, though further multi-centric larger trials are needed to replicate such findings in near future.

Funding: Nil, **Conflict of interest:** None initiated, **Perission from IRB:** Yes

References

1. Aulakh R, Tiwari A. Subacute sclerosing panencephalitis in a toddler: changing epidemiological trends. Case Rep Pediatr. 2013;341462. doi: 10.1155/2013/341462. Epub 2013 Dec 12.

2. Saha V, John TJ, Mukundan P, Gnanamuthu C, Prabhakar S, Arjundas G, et al. High incidence of subacute sclerosing panencephalitis in south India. Epidemiol Infect. 1990; 104:151–6

3. Bellini WJ, Rota JS, Lowe LE, Katz RS, Dyken PR, et al. Subacute sclerosing panencephalitis: more cases of this fatal disease are prevented by measles immunization than was previously recognized. J Infect Dis 2005; 192:1686–1693.

4. del Toro-Riera M, Macaya-Ruiz A, Raspall-Chaure M, Tallada-Serra M, Pasqual-López I, Roig-Quilis M et al. Subacute sclerosing panencephalitis: combined treatment with interferon alpha and intraventricular ribavirin. Rev Neurol. 2006 Mar 1-15;42(5):277-81.

5. Hara S, Kimura H, Hoshino Y, Hayashi N, Negoro T, Okumura A, et al. Combination therapy with intra-ventricular interferon-alpha and ribavirin for subacute sclerosing panencephalitis and monitoring measles virus RNA by quantitative PCR assay. Brain Dev.2003 Aug; 25 (5):367-9.

6. Hosoya M, Mori S, Tomoda A, Mori K, Sawaishi Y, Kimura H. Pharmacokinetics and effects of ribavirin following intraventricular administration for treatment of subacute sclerosing panencephalitis. Antimicrob Agents Chemother. 2004 Dec;48(12):4631-5.

7. Ghosh K.C, Bhattacharya R, Ghosh S, Mahata M, Das S, Das S, Mondal G.P. Comparative study of the outcome ofpediatric subacute sclerosing pan-encephalitis patients treated with oral ribavirin versus intraventricular interferon alpha 2b via Ommaya reservoir. Int J Pediatr Res. 2018;5(6):320-325.doi: 10.17511/ijpr.2018.6.04.

8. Miyazaki K, Hashimoto K, Suyama K, Sato M et al. Maintaining Concentration of Ribavirin in Cerebro-spinal Fluid by a New Dosage Method; Three Cases of Subacute Sclerosing Panencephalitis Treated Using a Subcutaneous Continuous Infusion Pump. Pediatr Infect Dis J. 2018 Aug 27. doi: 10.1097/INF. 00000000 00002181. [Epub ahead of print]

……..

How to cite this article?

Aulakh R. Subacute sclerosing panencephalitis: promising results with intraventricular interferon alpha 2b therapy and intraventricular ribavarin therapy. Int J Pediatr Res. 2018;5(6):306-307.doi:10.17511/ijpr.2018.i06.01.

…….....