Editorial

Clinical Neurological Research in Children

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Introduction

Child neurology has evolved into a specialty of cutting-edge treatments targeted at curing disease at its source. The authors of this article discuss some of the most modern treatments that have changed degenerative and deadly ailments into chronic illnesses. Therapy in child neurology has a bright future, and practising child neurologists must comprehend the concepts of these novel therapies. The molecular understanding of the pathogenic pathways behind children's neurologic illnesses has sparked a tremendous period of research into disease aetiology. This research's promise has come true in the form of cures and therapies that address underlying deficits. The rapid pace at which new research is being presented promises to herald in a shift in child neurology from a diagnostic and supporting discipline to one that is interventional.

Techniques

■ Antisense Oligonucleotides (ASO)

Antisense Oligonucleotides (ASOs) are tiny DNA molecules that can change the expression of RNA and proteins, target mutant alleles, inhibit DNA silencing, and induce dosage effects. 3 The targeting and design of these ASOs are outside the scope of this chapter, but they have been extensively researched. Human advantages of these small compounds, on the other hand, have been proven in spinal muscular atrophy, muscular dystrophy, and CLN7-related Batten disease in an N-of-1 research.

Children with spinal muscular atrophy can't create enough Survival Motor Neuron (SMN) protein to keep their anterior horn cells alive. SMN1 transcription can create this protein, whereas SMN2 transcription is less efficient. Nusinersen alters SMN2 transcripts (splicing) to improve the efficiency of the SMN protein, reducing illness development and, in certain situations, enhancing neurologic function. Loss-of-function mutations in Dystrophin cause Duchenne muscular dystrophy. This gene is lengthy (79 exons), and disease is frequently caused by premature stops caused by mutations. ASOs meant to treat Duchenne have been successful in producing some protein by skipping exons in a personal mutation-specific manner.

■ Enzyme replacement

Somatic diseases caused by enzyme deficits can be treated with intravenous enzyme infusions, making enzyme replacement a common treatment option for somatic disorders. Because most proteins do not penetrate the blood-brain barrier, replacing enzymes in the brain remains difficult. As a result, enzyme replacement for brain illness is and will continue to be difficult. Cerliponase alfa, a recombinant tripeptidyl peptidase (actually generated as a proenzyme), is the first enzyme replacement therapy to be approved for a human neurologic illness, late infantile neuronal ceroid lipofuscinosis (CLN2-related Batten disease). This treatment is an enzyme replacement administered every two weeks via a ventricular port in humans, inspired on a treatment of a naturally occurring Beagle model of late infantile neuronal ceroid lipofuscinosis. It causes the illness, which is a rapidly developing neurological disorder, to come to a halt. Because the medication has just been

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available for roughly 5 years, it is unclear if it will merely prevent brain disease or allow sickness to spread to the eyes or other tissues. Because this is an enzyme substitute, reactions are prevalent, as they are with other enzyme substitutes.

■ Gene Introduction

Several recent clinical trials, including a revolutionary one to treat spinal muscular atrophy, have used adeno-associated viruses (AAV) to transfer genes into the central nervous system (CNS). Much of the criticism of this strategy has centred on how effective these vectors are at introducing genes into neurons.

Although the effectiveness of an AAV-9-mediated introduction of SMN into the CNS of patients with spinal muscular atrophy is still debatable, the efficacy of an AAV-9-mediated introduction of SMN into the CNS of patients with spinal muscular atrophy has been drastically proven.