Abstract
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Role of Gene replacement therapy in children have infantile and later onset spinal muscular atrophy (SMA): survival, motor function, motor milestone, clinical endpoints and safety profile

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Abstract

Spinal muscular atrophy (SMA) is a neurodegenerative disease involving the deletion of the SMN1 gene. Traditional treatment is primarily supportive. In 2019, the FDA approved gene therapy in children to improve quality of life and prolong survival. This article aims to study the efficacy and safety of different gene replacement therapies in children with SMA. This systematic review and meta-analysis was conducted according to PRISMA-P and the recommendations of the Cochrane Collaboration Handbook. An electronic search was conducted in MEDLINE, PubMed, Google Scholar, and Clinicaltrials.gov using the keywords: 'gene therapy', 'SMA', 'Nusinersen', 'AVXS_101', 'AVV' and 'spinal muscular atrophy'. A total of eight studies were included for analysis. Significant difference between antisense oligonucleotide (nusinersen) and onasemnogen abeparvovec (AVXS-101) was seen in mortality rate RR 0.42 (95% CI 0.23-0.78, p=0.006, I2 = 0%). While no difference was seen for survival outcome RR 1.19 (95% CI 0.17-8.54, p=0.086, I2 = 97%), permanent assisted ventilation RR 1.43 (95% CI 0.17-12.20, p= 0.75, I2 = 62%). Comparing nusinersen vs placebo; no difference is seen in adverse effects RR 0.96 (95% CI 0.91- 1.01, p = 0.15, I2 = 21%) but in regards to severe adverse events nusinersen is favored RR 0.37 (95% CI 0.17-0.81, p = 0.01, I2 = 0%). In general, gene therapy for SMA is shown to be well tolerated with significant improvement in motor function, and achievement of developmental milestones evidenced in the studies of Chiriboga et al., Al-Zaidy et al., Waldrop et al. and Mendell et al. However, a clinical trial by Biogen investigated the dose dependent efficacy and safety of nusinersen where 81.2% of subjects on high dose received a fatal outcome. Waldrop et al. also noted 90% of patients had an asymptomatic drop in platelets in the first week of treatment with AVXS-101. Gene replacement therapy potentially improves mortality rate and motor function, extends overall survival and increases CHOP and HFMSE scores. However, further long-term controlled trials are necessary to evaluate the efficacy and risk related factors among pediatric patients.

Biography

Alla Hamdan has done MBBS from Omdurman Islamic university, Sudan. She is a Registrar of pediatrics at Sudan medical specialization board (S.M.S.B). She is also a Research collaborator at Larkin community hospital division of clinical and transitional research, south Miami, Florida, USA