Restorative treatments of dystrophin expression in Duchenne muscular dystrophy: A systematic review
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Background:

•Duchenne muscular dystrophy (DMD) is a severe X-linked recessive disease.
•Corticosteroids is only known therapy known to cause delay in disease progression
•In recent year therapeutic strategies targeting increasing expression of dystrophin protein have reported promising results. Ataluren (non-sense exon skipping), Eteplirsen, Drisapersen, Casimersen, Viltolarsen and Golodirsen have been studied.
•Ataluren and Eteplirsen have been conditionally approved by EMA and FDA.

Methodology:

•Systematic review and metanalysis of randomized controlled trial
•Published from inception to December 2019
•Clinical trials addressing the effect of restorative treatments of dystrophin expression in children with DMD on functional outcomes, 6 minute walk distance (6MWD) and other timed function tests (TFT's)
•Dersimonian-laird method was used to calculate the pooled estimates for functional outcomes.

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Restorative Treatments of Dystrophin expression in Duchenne Muscular Dystrophy: A Systematic Review

Results:

- Eleven studies included in the systematic review, and five included in the meta-analysis.
- A total 917 boys with DMD, with mean age ranging from 6.9 to 13.1 years were included
- Four studies analyzed the effect of eteplirsen, three drisapersen, one casimersen, two ataluren, and one gentamicin.
- Eteplirsen showed a significant positive effect on 6MWD, with a mean difference of (Δ6MWD) 67.3 and 151.0 m, at 48 weeks and 3 years respectively
- The pooled mean difference for ataluren in the 6MWD test was (Δ6MWD) 18.3m (95% CI: 1.0, 35.5) and for drisapersen 21.5 m (95% CI: 4.7, 38.3).
- Ten of the included studies assessed the effect of treatments on secondary outcomes (dystrophin expression, exon skipping, cardiorespiratory function, or biochemicalchanges), and all the treatments improved dystrophin expression, respiratory function, and biochemical changes.

Conclusion: There is limited evidence for effectiveness of the newer therapies in DMD. Pooled analysis showed ataluren and Drisapersen improved 6MWD. Eteplirsen and Ataluren could modestly reduce disease progression. However, more trials are needed to confirm the efficacy, quality of life and cost effectiveness.

EXPERT COMMENT

"Dystrophin restorative therapies are aimed to increase the dystrophin expression in the muscles, and in terms expected to improve functional outcome of boys with DMD. A modest improvement in 6MWD was observed with Ataluren, Etepilrsen and Drisapersen. Long term studies are required to verify the real effect on functional outcomes and improvement in the quality of life."

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Reference

Pascual-Morena C, Cavero-Redondo I, Álvarez-Bueno C, Mesas AE, Pozuelo-Carrascosa D, Martínez-Vizcaíno V. Restorative treDr Renu Suthar MD, DM (Pediatric Neurology) Associate Professor, Department of Pediatrics, PGIMER, Chandigarhatments of dystrophin expression in Duchenne muscular dystrophy: A systematic review. Ann Clin Transl Neurol. 2020 Sep;7(9):1738-1752.