Disease modifying therapies in Spinal Muscular Atrophy – A Single Centre Experience

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INTRODUCTION

- Spinal Muscular Atrophy(SMA) : Rare genetic neuronopathy l/t progressive muscle weakness & atrophy
- Incidence: **1 in 10000** live births
- Commonest fatal genetic disease of infants
- Types 0-4, high mortality in early onset types
- New disease modifying therapies have shifted the paradigm in treatment of SMA

Nusinersen; Intrathecal (2016) → Onasemnogene abeparvovec; IV (2019) → Risdiplam;oral (2020)

- Available only at few centres in India resulting to limited data on these agents

OBJECTIVES

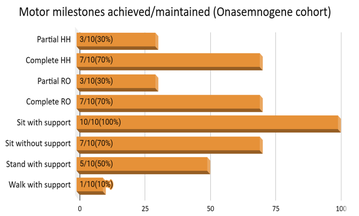
- To assess efficacy & adverse effect profile of Onasemnogene and Risdiplam in SMA patients of a tertiary care centre in Mumbai ,India

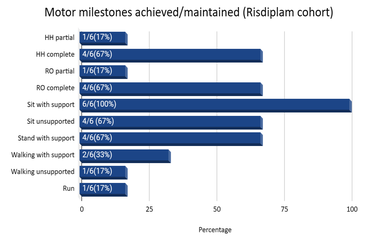
MATERIALS & METHODS

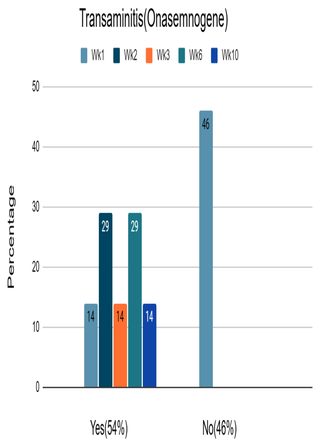
- Study Type & duration: Ambispective cohort study. Commenced in Jan 2023 to March 2024
- Ethical clearance and informed consent taken
- Inclusion criteria: All SMA patients who received either Onasemnogene(<2 yrs) &/or Risdiplam b/w Feb 2021 to December 2023 had adequate medical records and consented for regular follow up
- Exclusion Criteria; Follow up duration of **<3 months**
- Patients were ambispectively followed up for a period of minimum **3 months to maximum 3 years**
- Validated scales used: **CHOP INTEND** (Children's Hospital of Philadelphia Infant Test of Neuromuscular disorder) & **HFMSE** (Hammersmith Functional Motor Scale Expanded) for evaluation of motor function
- Data collected by review of past medical records, interview & examination; Data analyzed by Microsoft Excel version 2021
- Qualitative variables expressed as number and percentage while quantitative variables as median/SD

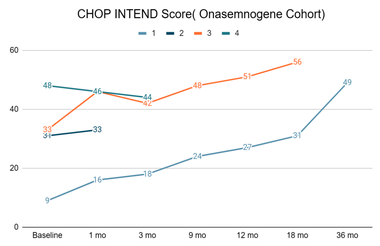
RESULTS

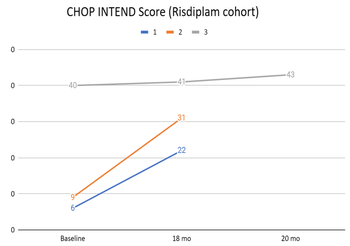
- Onasemnogene (n=13); Risdiplam(n=7), Out of these 2 patients received Onasemnogene f/b Risdiplam
- Onasemnogene cohort: **3 expired**,Risdiplam Cohort: 1 lost to follow
- Thus 10 patients of Onasemnogene and 6 patients of Risdiplam were ambispectively followed for outcome
- Adverse effect was studied in the entire cohort
- Median age of receiving therapy: Onasemnogene: 18±7 mo(6 mo-23 mo), Risdiplam: 4±2 yrs(6 mo-8 yrs)
- Sitting with support in all patients of both cohort
- Highest milestone achieved/maintained: Onasemnogene: Walking with support (**10%**); Risdiplam: Running (**17%**)
- Motor scores: **Improved** in most patients with maximum increase of **40** points in Onasemnogene & **22** points in Risdiplam cohort. However, it **worsened in 3** patients d/t knock knee, discontinuation of physiotherapy, and a different OT evaluating score respectively
- Respiratory support was needed only in one patient at baseline(SMA1) which could be withdrawn **2.5 yrs** after therapy (Onasemnogene f/b Risdiplam)
- Feeding support could be withdrawn in 50% patients in both cohort, only one SMA type 1 patient remained dependent on PEG tube feeding even with Onasemnogene & Risdiplam therapy.
- **50%** patients in Onasemnogene cohort and **33%** in Risdiplam cohort were **admitted** d/t respiratory tract infection even after therapy
- **Scoliosis** worsening was noted in **30% &33%** patients of Onasemnogene and Risdiplam cohort respectively, one patient even underwent scoliosis surgery, others managed conservatively
- Adverse effects: Omasemnogene: Most common: **Transaminitis** 54%, Thrombocytopenia 23%; Frequent respiratory tract infection in 1 patient of Risdiplam cohort

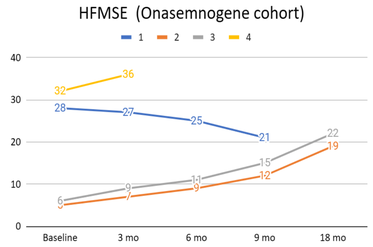


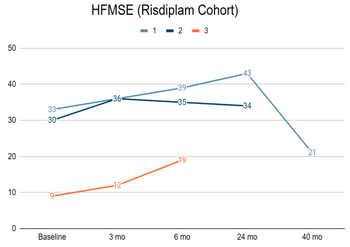












CONCLUSION

- Newer disease modifying agents do appear **beneficial** in SMA: improve survival as well as motor milestones
- **Early treatment** leads to better outcome
- **Ongoing rehabilitation** despite new agents plays a crucial role
- **Exorbitant cost, poor availability and potential adverse effects** are some of the limitations of these therapies
- Very few single centre studies on outcome of these therapies apart from the well known clinical trials
- This study throws light on the **Indian scenario**, where availability and affordability is a major **barrier**
- All attempts should be made to break this barrier so that more patients can be benefited

REFERENCES

- Spinal Muscular Atrophy - Symptoms, Causes, Treatment | NORD (2022)
- Naveed A,et al; J Pediatr Pharmacol Ther (2021)
- Kakazu J,et al; Orthop Rev (2021)

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