INPLASY PROTOCOL

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Corresponding author:
Xinyu Gu

16301050069@fudan.edu.cn

Author Affiliation:
Huashan Hospital, Fudan University.

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Review Stage at time of this submission: **Data analysis.**

Conflicts of interest:
None declared.

The clinical manifestations and treatment strategies of congenital myasthenic syndrome associated with endplate development and maintenance deficiency: a systematic review and meta-analysis of case reports and case series

Gu, XY[1]; Zhao, CB[2]; Xi, JY[3].

Review question / Objective: **We aimed to investigate the demographic features, clinical manifestations and treatment strategies of CMS associated with the Agrin/LRP4/MuSK/Dok7/Rapsyn signaling pathway.**
Condition being studied: **As with all other rare disorders, there has been few large cohort study or clinical trials focusing on CMS associated with endplate development and maintenance deficiency. In such case, systematic reviews are required to help guide the clinician's diagnostic test and therapeutic strategy, so as to avoid misdiagnosis and inappropriate treatment.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 March 2023 and was last updated on 23 March 2023 (registration number INPLASY202330085).

INTRODUCTION

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CMS associated with endplate development and maintenance deficiency. In such case, systematic reviews are required to help guide the clinician's diagnostic test and therapeutic strategy, so as to avoid misdiagnosis and inappropriate treatment.

METHODS

Participant or population: Patients who were genetically confirmed as congenital myasthenic syndrome associated with AGRN, LRPS4, MUSK, DOK7 or RAPSN mutation.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: Case reports and case series.

Eligibility criteria: Additional inclusion criteria: Genetic tests confirmed the AGRN, LRP4, MUSK, DOK7 or RAPSN mutations regardless of the details of the mutations; Additional exclusion criteria:1. Genetic test not performed; 2.Lack of clear descriptions of clinical manifestations or pharmacological treatment.

Information sources: PubMed, MEDLINE, Web of Science, Cochrane Library databases.

Main outcome(s): A beneficial effect of acetylcholinesterase inhibitor (AChEI) was found on RAPSN patients. In patients with AGRN, LRP4, MUSK and DOK7 cases, beta-adrenoceptor agonist displayed the best treatment effect, whereas AChEI often leads to non-improvement or deteriorations.

Quality assessment / Risk of bias analysis: A validated tool for the determination of the methodological quality of the case reports and case series proposed by Murad et al. based on the previous criteria from Pierson, Bradford Hills, and Newcastle-Ottawa scale modifications was used. Each case report or series was evaluated by two authors under 4 domains (selection, ascertainment, causality, and reporting). This resulted in 8 leading exploratory questions with a binary response (Yes/No) to determine whether the item was suggestive of bias or not.

Strategy of data synthesis: Patient demographic and clinical features were summarized descriptively. Comparisons were analyzed by GraphPad Prism 8, using Student t-test or Man Whitney U test depending on the type of data distribution. Multivariable conditional logistic regression was conducted using STATA software (Version 12.0, StataCorp LP, College Station, Texas), and results were reported as odds ratios (OR) with a 95% confidence interval (CI). A 2-sided $P < 0.05$ was considered statistically significant.

Subgroup analysis: Not applicable.

Sensitivity analysis: Not applicable.

Country(ies) involved: China.

Keywords: congenital myasthenic syndrome; neuromuscular junction.

Contributions of each author:
Author 1 - Xinyu Gu - Author 1 drafted the manuscript and analyzed the data.
Email: 16301050069@fudan.edu.cn
Author 2 - Chongbo Zhao - Author 2 conceptualized study and supervised the project.
Email: chongbozhao@fudan.edu.cn
Author 3 - Jianying Xi - Author 3 conceptualized study and supervised the project.
Email: xijianying@fudan.edu.cn