Swallowing outcomes in dysphagia interventions in children with Spinal Muscular Atrophy: protocol for a scoping review

Sofia Gandolfi,* Chiara Andriani and Margaret Walshe

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Abstract

Background: Spinal Muscular Atrophy (SMA) is a genetic neuromotor disease characterized by muscle weakness and atrophy. Among the clinical manifestations, swallowing difficulties can be associated with this disease and have a significant impact on pulmonary health, malnourishment, and aspiration pneumonia.

Swallowing-related outcomes selected for measurements differ from protocol to protocol in clinical research studies, which makes it hard to identify commonalities across different studies and apply standardized swallowing interventions.

Objective: This research aims to explore the characteristics of swallowing-related outcomes in clinical research in children with SMA to contribute to future research about dysphagia management in this population.

Methods: All research studies exploring clinical interventions for swallowing difficulties in children below 18 years of age with dysphagia associated with SMA will be included. Five electronic databases (EMBASE, CINAHL Complete, PubMed, Web of Science, and PsycInfo) will be searched, with no restrictions on dates, language, or type of study. Two independent reviewers will assess articles to meet the following criteria: 1) dysphagia intervention studies in children with SMA; 2) outcomes of dysphagia intervention; 3) methods of measurement of outcomes; 4) timepoints and frequency of measurement.

Conclusions: Examining the outcomes of dysphagia intervention in children with SMA will help identify the gaps in the literature and raise awareness about the lack of agreement in the management of swallowing difficulties experienced in this population, laying the foundations for future research to expose outcomes that are neglected.

Keywords: Dysphagia, Spinal Muscular Atrophy, Rehabilitative Interventions, Outcomes, Scoping Review

*Corresponding author: Sofia Gandolfi, Department of Clinical Speech and Language Studies, Trinity College Dublin, 7-9 South Leinster St, Dublin, Ireland, e-mail: gandolfs@tcd.ie

Introduction

Spinal Muscular Atrophy (SMA) is an autosomal recessive neuromuscular disease characterized by "muscle wasting, weakness, and feeding and respiratory difficulties" [1] (p. 706) , due to the lack of SMN protein, caused by the deletion of the survival motor neuron gene 1 (SMN1). The natural history of people with this condition has dramatically changed in the last decade thanks to three new pharmacological therapies: Spinraza® [2], Zolgensma® [3], and Evrysdi® [4]. All these therapies compensate for the lack of SMN protein, locally. Spinraza© is injected in the cerebrospinal fluid – or systemically– Zolgensma© is infused intravenously and Risdiplam© is given orally. Life expectancy has increased. A phase I/II trial showed that 15/15 patients were alive at 20 months old compared to the 8% of the natural history cohort [5]. New aspects of SMA management need to be taken into account [1] due to the development of aspects of the disease that before treatment were treated just through palliative care. One of the central issues is now the swallowing ability of babies with SMA since its impairment (dysphagia) can increase their risk of developing malnutrition, failure to thrive, and pulmonary complications [6]. Dysphagia severity varies among the SMA types and it is correlated with the patients' ability to hold their head and to control their trunk position, with weakness of respiratory muscles and the consequent inhibition of cough strength and clearance of lower airway from pathogens and aspirated materials, and with severe scoliosis [7]. "Despite the appreciated significance of bulbar impairment, there has historically been little systematic evaluation of its integrity within the clinical arena" [8] (p. 640). According to a Cochrane review of 2016, the main dysphagia interventions in progressive muscular disease are swallowing rehabilitation techniques, diet modification, and enteral feeding. However, there is "insufficient and low-quality RCT evidence to determine the effect of interventions for dysphagia in longterm, progressive muscle disease" [9] (p. 2). A direct consequence is the lack of a uniform approach to measuring swallowing-related outcomes, a common issue in other diseases with associated dysphagia, like head and neck cancer and airway reconstruction due to laryngotracheal stenosis [10]; [11]; [12]; [13]. From the research conducted in head and neck cancer, it emerged that the lack of comparability limits the possibility of conducting meta-analysis and data pooling. Furthermore, outcomes, which should cover all physical, psychological, social and contextual components of swallowing, are mainly focused on the anatomical factors [13]; [14].

Since there is no agreement on the management of swallowing difficulties in children with SMA, it is important to examine what are the targets of dysphagia intervention programmes, and to identify and analyse gaps in the existing research literature.

This research aims to explore the characteristics of swallowing-related outcomes in clinical research in children with SMA to contribute to future research about dysphagia management in this population.

The primary research questions for-

mulated using the Population Concept and Context (PCC) framework recommended by the Joanna Briggs Institute (JBI) updated methodological guidance [15] are:

1. Which swallowing-related outcomes are examined in dysphagia intervention studies involving children with SMA?

2. How are the swallowing-related outcomes in these studies defined?

3. How are the swallowing-related outcomes in these studies measured?

4. At which timepoints and at which frequency are the swallowing-related outcomes in these studies measured?

Methods

Having taken the scarcity of research in this area and its complex and heterogenous nature into account, a scoping review approach was considered suitable to understand what has been previously researched and what is the up-to-date evidence on outcomes in dysphagia intervention in children with SMA, incorporating various types of literature without critical appraisal [16].

To inform this review and increase the rigor and clarity of the review process, the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines [17] and the JBI updated methodological guidance [15] were used, and a study design was formulated using the JBI methodology for Scoping Reviews [18].

See Appendix A for an overview of the eligibility criteria following the Population Concept and Context (PCC) framework recommended by the JBI updated methodological guidance [15], based on Arksey and O'Malley's methodological framework [19].

Search strategy

The JBI three-step search strategy [18] will be utilised (see Table 1) by the PI to select potentially relevant studies.

The first step consists of a limited search in PubMed and CINAHL Complete, with a subsequent analysis of titles, abstracts and index terms, after which a comprehensive search string is developed by the Principal Investigator (PI). An iterative process of search string modification with any relevant new terms identified through the pilot search leads to an ultimate comprehensive search string. This is applied to five electronic databases (EMBASE, CINAHL Complete, PubMed, Web of Science, and PsycInfo), selected on the basis of the multidisciplinarity of journals. SMA is better managed in a multidisciplinary context, requiring a full team of professionals, since most of the main characteristics of SMA – head balance, trunk control, scoliosis, posture, weakness of facial, pulmonary, and limb muscles – impact multiple activities of daily living. Therefore, study design, language, or date of studies are not considered criteria for exclusion. See Appendix B for search strings. To cover all eligible articles, reference lists of all included studies are screened (step 3). Literature reviews, best practices rec-

ommendations and consusensus statements will be included as sources of additional studies. For full-text unavailability, it is planned that the PI will contact the primary authors.

In parallel with the electronic database search, grey literature will be searched to "minimize the effects of publication bias" [20] (p. 234) and to gain "a more balanced understanding of the evidence and a more accurate effect size" [20] (p. 234) . Among the grey literature databases, Wonder, Scopus, and Mednar are consulted by the PI for relevant articles and reviews, without the application of filters, aiming to cover the broadest possible area of existing literature.

Table 1: Three-step search strategy

Stage	Description
Stage 1	CINAHL Complete and PubMed are initially searched, and text words contained in titles, abstracts and index terms of found articles are analysed.
Stage 2	All included databases (EMBASE, CINAHL Complete, PubMed, Web of Science and PsycInfo) are searched through the implemented search string.
Stage 3	All reference lists of articles are screened for additional sources.

Study selection

Once the search is finalised, the relevant articles will be downloaded and exported to the citation manager Endnote software [21] for data storage and management. Then screening of abstracts of all articles and, subsequently, of the full texts of the articles that both the PI and the co-investigator (CA) selected as relevant will be carried out in Covidence [22], where duplicates are removed. First, a pilot screen will be independently performed by the PI and the co-investigator, in order to enhance consistency and reliability of the ScR. Having discussed results and refined eligibility criteria, both reviewers will first proceed to independently screen titles and abstracts, and then move on to full-texts, on the basis of eligibility criteria. Disagreements on study selection will be solved through discussion between investigators and consultation with the research supervisor. Grey literature will be searched by the PI and abstracts of all articles meeting the eligibility criteria will be revised by both the PI and the co-investigator. The selection process will be reported using the PRISMA flow diagram.

Data extraction

Covidence will be used to develop a data charting form, based on the research aim and objectives, examining the part of articles considered eligible from the full-text selection, to determine the main information to be extracted. In order to enhance the ScR validity and reliability, a pilot data charting will be independently completed by the PI and the co-investigator; then results will be discussed, and the data-charting form

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will be updated in an iterative process. Any disagreement will be discussed among the PI, the co-investigator, and the research supervisor to meet all data charting recommendations.

The following data will be extracted: study characteristics, type of evidence, population details, dysphagia intervention program, definition of outcomes, outcomes measures, frequency, and timepoints of measurements.

Data Analysis and Presentation

To answer all research questions, quantitative data extracted from studies will be mapped independently, and accompanied by frequency counts and percentage analysis of concepts, populations, and locations of studies, by the PI and the co-investigator. Together they will come up with an agreement and determine the final results.

According to the updated guidelines for conducting scoping reviews, "Scoping reviews do not undertake data synthesis such as statistical meta-analysis, following assessment of the methodological quality, heterogeneity, or risk of bias of included studies" [23] (p. 964), since "little value would be gained in performing such an analysis" [15] (p. 2125). Hence, a data synthesis will not be carried out.

Discussion

There is very little research done in this area. Hence, examining what outcomes are selected for dysphagia intervention in children with SMA will help the PI understand what is important to research, identify the gaps in the literature and raise awareness about the lack of agreement in the management of swallowing difficulties experienced in this population, laying the foundations for future research to expose outcomes that are neglected, identifying their definition, the measurement tools and the timepoints of outcome measurement.

This may result in strengthening the evidence in dysphagia intervention in children affected by SMA, reducing heterogeneity between studies.

Acknowledgments

Declaration of Interest

Abbreviations

CINAHL = Cumulative Index to Nursing and Allied Health Literature, EMBASE = Excerpta Medica database, JBI = Joanna Briggs Institute, PCC = Population Concept Context, PI = Principal Investigator, PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta Analysis extension for Scoping Reviews, ScR = Scoping Review, SMA = Spinal Muscular Atrophy

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Appendices

Appendix A: Eligibility criteria

Inclusion	Criteria	Rationale	Exclusion	Criteria	Rationale
Population					
Infants, children, and adolescents	0-17.11 years	Swallowing difficulties have been reported in all SMA type 1, 2 and 3 (Dunaway Young et al., 2023), whose symptoms arise by 18 years.	Adults	Above 18 years	There is no evidence of swallowing problem in people with SMA type 4, developed in adulthood.

Inclusion	Criteria	Rationale	Exclusion	Criteria	Rationale
Concept					
Dysphagia interventions	Dysphagia interventions, composed of direct, indirect and compensatory interventions, consist of motor and sensory swallowing exercises, motor and sensory exercises without bolus consumption, compensatory swallowing strategies (including posture considerations), bolus consistency modification, and caregiver/patient education.	Dysphagia can cause respiratory distress, pneumonia, poor weight gain and dehydration and it is a frequent source of infant mortality in this population. Dysphagia intervention could have significant impact on airway protection and pharyngeal clearance.	Medical interventions	Botulinum toxin, upper oesophageal dilatation and cricopharyngeal myotomy	The main purpose of this ScR is to identify the dysphagia rehabilitation outcomes. Medical interventions do not provide information on this topic.

Inclusion	Criteria	Rationale	Exclusion	Criteria	Rationale
Context					
All types of study designs and grey literature	All forms of experimental and observational studies, and literature reviews. Grey literature includes academic papers, thesis and dissertations, research and committee reports, government reports, conference papers, and ongoing research.	To cover a broad range of evidence and minimise the effects of publication bias.	-	-	-
All clinical contexts, languages, dates, cultures, ethnicities	No contextual specific restriction	To enhance comprehensiveness of the ScR.	-	-	-

Appendix B: Search strings for all databases

Stand 1	"spinal muscular atrophy"
Strand 2	swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food*
Database	Search string
Pubmed	("muscular atrophy, spinal"[MeSH Terms] OR "Spinal Muscular Atrophies of Childhood"[MeSH Terms] OR "spinal muscular atrophy"[Title/Abstract]) AND ("Deglutition Disorders"[MeSH Terms] OR ("swallow*"[Title/Abstract] OR "deglutition*"[Title/Abstract] OR "dysphagi*"[Title/Abstract] OR "eats"[Title/Abstract] OR "eating"[Title/Abstract] OR "ate"[Title/Abstract] OR "eat"[Title/Abstract] OR "drink*"[Title/Abstract] OR "drank"[Title/Abstract] OR "feed*"[Title/Abstract] OR "fed"[Title/Abstract] OR "food*"[Title/Abstract]))
EMBASE	('spinal muscular atrophy'/exp AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) OR 'spinal muscular atrophy':ab,ti) AND ('dysphagia'/exp AND [embase]/lim NOT ([embase]/lim AND [medline]/lim) OR swallow*:ab,ti OR deglutition*:ab,ti OR dysphagi*:ab,ti OR eats:ab,ti OR eating:ab,ti OR ate:ab,ti OR eat:ab,ti OR drink*:ab,ti OR drank:ab,ti OR feed*:ab,ti OR fed:ab,ti OR food*:ab,ti) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

Database	Search string
CINAHL Complete	((MH "Muscular Atrophy, Spinal") OR TI "spinal muscular atrophy" OR AB "spinal muscular atrophy") AND ((MH "Deglutition Disorders") OR TI (swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food*) OR AB (swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food*)) Limiters - Exclude MEDLINE records
Web of Science	"spinal muscular atrophy" (Topic) and swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food* (Topic) and Preprint Citation Index (Exclude – Database) and MEDLINE® (Exclude – Database)
Psycinfo	(TI "spinal muscular atrophy" OR AB "spinal muscular atrophy" OR DE "Muscular Atrophy") AND (TI (swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food*) OR AB (swallow* OR deglutition* OR dysphagi* OR eats OR eating OR ate OR eat OR drink* OR drank OR feed* OR fed OR food*) OR DE "Dysphagia")