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SYSTEMATIC REVIEW

Dysphagia, dysphonia and olfactory disease: a map of Cochrane evidence relevant to rehabilitation for people with post COVID-19 condition

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ABSTRACT

INTRODUCTION: Currently, no evidence exists on specific treatments for post COVID-19 condition (PCC). However, rehabilitation interventions that proved effective for similar symptoms in other health conditions could be applied to people with PCC. With this overview of systematic reviews with mapping, we aimed to describe the Cochrane evidence on rehabilitation interventions proposed for dysphagia, dysphonia and olfactory dysfunction in different health conditions that can be relevant for PCC.

EVIDENCE ACQUISITION: We searched the last five years' Cochrane Systematic Review (CSRs) using the terms "dysphagia," "swallowing disorder," "dysphonia," "voice disorder," "olfactory dysfunction," "smell changes" and "rehabilitation" in the Cochrane Library. We extracted and summarized the available evidence using a map. We grouped the included CSRs for health conditions and interventions, indicating the effect and the quality of evidence.

EVIDENCE SYNTHESIS: We found 170 CSRs published between 2016 and 2021 and 1 was included. It provided data on dysphagia in acute and subacute stroke. Interventions included were acupuncture, neuromuscular electrical stimulation, transcranial magnetic stimulation and behavioral interventions, and swallowing therapy, with very low- to moderate-quality evidence. We did not find any CSR on dysphonia and olfactory disease.

CONCLUSIONS: These results are the first step of indirect evidence able to generate helpful hypotheses for clinical practice and future research. They served as the basis for the three recommendations on treatments for these PCC symptoms published in the current WHO Guidelines for clinical practice.

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KEY WORDS: Post-acute COVID-19 syndrome; Rehabilitation; Deglutition disorders; Dysphonia; Olfaction disorders.

Introduction

This short paper focused on dysphagia, dysphonia, and olfactory disease is part of a series developed by Cochrane Rehabilitation in collaboration with the World Health Organization (WHO) to identify the Cochrane evidence relevant to the treatment of symptoms related to the post COVID-19 condition (PCC).[1, 2] Although initially associated with respiratory and parainfluenza symptoms,[3] COVID-19 demonstrated a wide range of clinical

manifestations, including swallowing, olfactory, and voice dysfunctions.[4, 5] These symptoms were also related to the central and peripheral nervous system dysfunction caused by this viral infection. Many neurological manifestations, such as encephalopathy, Guillain-Barre Syndrome, seizures, and stroke, lead to dysphagia and dysphonia.[6, 7] Most studies reported dysphagia as a consequence of long oral-tracheal intubation, tracheostomy, neurological involvement, and critical illness status. While other authors observed similar conditions also in non-intubated ones linking this condition to pulmonary function alterations and viral neuronal activity.[8, 9] Dysphonia in PCC seemed to be related to respiratory dysfunction and pneumo-phonic coordination, which was exacerbated in patients who required mechanical ventilation. Other studies focused people with COVID-19. Laryngeal dysfunction and oedema were found in 66.7% of mechanically ventilated patients. Impaired airway protection and glottis function were associated with longer artificial airway duration, longer tracheostomy tube duration, and multiple intubations.[10] Aziz Azzam *et al.* recently investigated the presence of dysphonia in a cohort of 106 COVID patients and reported that 79% of participants had these symptoms, while 18.8% were phonesthetic. In particular, they found vocal fold edema, swellings, ventricular hypertrophy and vocal fold immobility, associating such congestion with dysphonia symptoms.[11] Finally, olfactory dysfunction, which rapidly became a pathological hallmark of acute COVID infection,[12] seems to be present in the majority of cases (10-60% of those initially affected) with little or no recovery during the first months.[13, 14] Despite the relevant impact of this condition on a person's social skills, relationships, well-being, and quality of life, its etiology is not well established.[14, 15] No specific treatments have been validated for these symptoms in PCC, but some interventions have already been applied for such disorders in the rehabilitation field. With the present review, we aimed to overview and provide a map of the current Cochrane evidence on the efficacy of rehabilitation treatments proposed for dysphagia, dysphonia, and olfactory dysfunction in other health conditions. The findings could fill, at least partially, the current knowledge gap in the management of these PCC otolaryngology deficits and provide clinicians with valuable tools for delivering appropriate treatments. Results from the present review can also contribute to generating new research questions for future primary studies.

Evidence acquisition

The design of this study is an overview of reviews with mapping. We reported the methods used in a previous publication.[2] In this short paper, we included Cochrane Systematic Reviews (CSRs) relevant to PCC that considered dysphagia, dysphonia, and olfactory dysfunction, as defined by the WHO.[1] We summarize the search string in Table I.

Evidence synthesis

Dysphagia

We screened 170 CSRs, excluding 39 at the title and abstract stage. We screened 131 full texts, with 1 CSR that met the inclusion criteria (Supplementary Digital Material 1: Supplementary Table I). Participants were adults with acute and subacute stroke with dysphagia. A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2 assessment reported a high methodological quality for the CSR included (Supplementary Digital Material 2: Supplementary Table II). The review[16] also evaluated the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. We categorized the swallowing interventions among the following main treatments: acupuncture, behavioral interventions, neuromuscular electrical stimulation (NMES), physical stimulation, transcranial direct cerebral stimulation (tDCS), and transcranial magnetic stimulation (TMS). There was moderate-quality evidence for the effect of swallowing therapy on case fatality and length of stay in hospitalized people with acute and subacute stroke. There was low-quality evidence on penetration aspiration score and dysphagia. Furthermore, there was very low-quality evidence on swallowing ability concerning chest infection

TABLE I.—*Impairment, related symptoms and outcomes relevant to post COVID-19 condition included in the study, as identified by WHO rehabilitation program.*

Impairment	Synonyms/variations	Outcomes
Dysphagia	Dysphagia, swallowing disorder	Subjective or objective assessment of dysphagia (*e.g.*, Dysphagia Severity Rating Scale; penetration aspiration score determined by videofluorographic swallowing study)
Dysphonia	Dysphonia, voice disorder	Not available Cochrane reviews corresponding to the search criteria
Olfactory dysfunction	Olfactory dysfunction, smell changes	Not available Cochrane reviews corresponding to the search criteria

Sources used for the selection of symptom: survey results from the Royal College of Speech and Language Therapists (UK).

TABLE II.—*Evidence map of interventions for dysphagia symptoms compared to control, sham intervention, no therapy.*

Treatment	Acute and subacute stroke									
	Aspiration	Case fatality	Chest infection or pneumonia	Disability	Dysphagia	Institutionalization	Length of stay	Nutritional (albumin)	Pharyngeal transit	Swallowing ability
Acupuncture					Na**					Na***
Behavioral intervention	Na**	Na***	Na**	M*	Na**	Na***	Na***	Na***		Na**
Neuromuscular electrical stimulation	Na***		Na***		Na***				Na	Na***
Pharyngeal electrical stimulation	Na***	Na***	Na***		Na***	Na***	Na***	Na***	Na***	Na***
Physical stimulation (thermal, tactile)		Na***			Na***				Na	Na***
Swallowing therapy	L*	M*	VL*		L*	Na***	M*	Na***	Na	VL*
Transcranial direct current stimulation										Na***
Transcranial magnetic stimulation	Na***	Na***			Na***					Na

Lines represent the interventions. Columns represent the health conditions where the searched outcome has been considered.
*Effect against the intervention; **effect in favor of the intervention; ***no definite results.
Quality of evidence was reported into each cell with the following acronyms: VL: very low-quality; L: low-quality; M: moderate-quality; H: high-quality; Na: not available.

and pneumonia (Table II). The effects of acupuncture were controversial; it effectively reduced the proportion of participants with dysphagia at the end of the trial. Nevertheless, no effect was found on swallowing ability. Behavioral interventions included various swallowing exercises, like environmental modifications, safe swallowing advice, dietary modifications, kinesio-taping, and expiratory muscle strength training. They are likely to be effective in reducing cases of penetration aspiration scores and improving swallowing ability. However, they did not positively affect institutionalization, lengths of inpatient stay, functional outcome, chest infection or pneumonia. NMES improved pharyngeal transit time but had no effects on swallowing ability, penetration aspiration score, and the proportion of participants with dysphagia. Pharyngeal electrical stimulation (PES) had no effects on the proportion of dysphagic patients, swallowing ability and no effects on penetration aspiration score, chest infections, pharyngeal transit time, institutionalization, length of inpatient stay and case fatality. Physical stimulation increased pharyngeal transit time, no effects proportion of dysphagic patients, case fatality and no swallowing ability. TDCS showed no effect on the proportion of dysphagic patients or swallowing ability. TMS improved swallowing ability, with no effects on case fatality and penetration aspiration score.

Dysphonia and olfactory dysfunction

We did not find CSRs that specifically addressed dysphonia or olfactory dysfunction.

Discussion

This paper overviewed and mapped the Cochrane evidence from different health conditions that could be relevant to managing dysphagia, dysphonia, and olfactory dysfunction in PCC. We found only one CSR related to swallowing rehabilitation in people with acute and subacute stroke. Swallowing therapy includes various interventions, like acupuncture, PES, NMES, TMS, behavioral interventions, and physical stimulation. Conversely, we did not find any Cochrane evidence about dysphonia and olfactory dysfunction management in the rehabilitation field. When implementing the "evidence relevant to," we need to check: 1) if there are specific pathophysiological mechanisms of PCC suggesting avoiding any of the identified treatments; and 2) if there are treatments specific for the reported health conditions that would not be appropriate for PCC. Obviously, in the implementation phase, the need to check individual contraindications in single patients remains. The WHO identified one red flag for PCC rehabilitation: postexertional symptom exacerbation.[17] This can represent an individual contra-indication for all the treatments considered below. Swallowing therapy showed a moderate effect on case fatality and length of stay in hospitalized people with acute and subacute stroke. These results are relevant because one of the most critical outcomes of rehabilitation in people with COVID-19 is fatality and the reduction of hospitalization and length of inpatient stay. Although the CSR focused on a stroke population, a multidisciplinary approach, including swallowing therapy, is likely to reduce hospitalization in people with post COVID-19. Given the severity of pneumonia in people with PCC aspiration of food into the airways has been recognized as one of the main factors associated with worsening pulmonary infections.[8] Behavioral treatments showed positive effects on penetration and aspiration of food in the selected CSR. Behavioral treatment involved swallowing

compensatory strategies (such as change of food consistency and postural maneuvers),swallowing therapy, non-invasive stimulations, environmental modifications, and educational training.[16] A recent cohort of studies in people with COVID-19 and swallowing disorders confirmed that modified food consistency and early speech and language intervention increased the recovery of this population.[10] Considering the considerable heterogeneity of PCC manifestations, this multi-component approach could provide beneficial effects using tailored strategies based on the specific needs of the patients. Moreover, behavioral interventions could result in habit change and greater self-management, promoting the maintenance of exercises and positive outcomes in the longer term.[18, 19] Accordingly, the CSR reported that behavioral treatments also enhanced the deglutition ability (skills to ingest food safely and efficiently). The CSR revealed that also TMS increased the swallowing skills in people with dysphagia and stroke. In literature, TMS has been recognized to have positive effects in people with cortical damage as it could enhance swallowing function by modulating cortical excitability,[20] for this reason, it could contribute to improving swallowing skills in people with COVID and cortical impairments. In literature, it is well recognized that critically ill patients with dysphagia can present with acquired weakness and atrophy of the skeletal musculature of the oropharynx; swallow-strengthening exercises, as well as peripheral neuromuscular electrical stimulation, could be physiologically reasonable and appropriate to use in this population. In Bath *et al.*, NMES positively affected the pharyngeal transit time, potentially reducing pharyngeal food residue. NMES is widely applied for the treatment of pain, muscle strengthening, and sensorimotor recovery enhancement.[21] It can be used to stimulate muscle contractions and activate neural pathways, reinforcing compromised oropharyngeal musculature and triggering muscle contraction by depolarizing nerve fibers on neck muscles.[22, 23] Furthermore, the CSR reported that acupuncture therapy could effectively reduce the proportion of patients with dysphagia. Nevertheless, it showed no effects on swallowing ability. This discrepancy should be further investigated.[24] In conclusion, despite the current lack of evidence in reporting swallowing therapy in people with PCC, some swallowing interventions could be effective also in the population with post COVID symptoms. In addition, given the complexity of COVID-19 and the severe sequelae of swallowing impairments, a multidisciplinary approach is necessary to treat dysphagic people with COVID-19. Looking at the indirect evidence provided with this work and at the current direct evidence coming from the rapid living systematic review produced by Cochrane Rehabilitation,[25-27] the experts conveyed by the WHO provided a conditional recommendation for the clinical rehabilitation management swallowing impairment in adults with PCC:[17] "we suggest using a combination of education and skills training on positioning, maneuvers and dietary modifications, and swallowing exercises."[17]

Limitations of the study

Our map of CSRs focuses on the best current evidence relevant to dysphagia, dysphonia, and olfactory intervention rehabilitation for people with PCC. However, other high-quality systematic reviews could not be considered in the selection process because they were not included in the Cochrane Library. We need to interpret the findings very carefully due to the inclusion of a single CSR on dysphagia, not reporting the GRADE evidence in many cases. This aspect has to be improved in future studies. In addition, our study did not specifically provide evidence on PCC dysphagia management but could provide useful information to bridge the knowledge gap on the topic. These findings can be helpful for clinicians in delivering more appropriate treatments for individual patients and promote the development of new dedicated studies.

Conclusions

Specific rehabilitation interventions successfully used in different health conditions may improve dysphagia in PCC. Future research priorities should include producing new and particular evidence on PCC and improving the methodological quality of primary studies in people with chronic diseases. Further, there is a need for CSRs to consider the symptoms of postexertional malaise and orthostatic intolerance.

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