Critical Review: Does prophylactic swallowing therapy for head and neck cancer patients result in the reduction of chemoradiation and/or radiation treatment-related dysphagia?

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This critical literature review examines the evidence regarding prophylactic swallowing therapy for head and neck cancer (HNC) patients that undergo chemoradiation and/or radiation therapy, and its impact on treatment-related dysphagia.

Introduction

Head and neck cancer has recently drawn more attention in research, as it is now the 7th most commonly occurring cancer in the world (Rettig & D'Souza, 2015). Radiation and chemoradiation therapy are forms of non-surgical treatment for head and neck cancer, but they often have acute and/or long-term effects on swallowing physiology, and can result in treatment-related dysphagia. Dysphagia is when a person has difficulties moving bolus from their mouth to their stomach. Treatment-related dysphagia can result in aspiration, a dependence on feeding tubes for nutrition, and nutritional deficiencies (Murphy & Gilbert, 2009).

Traditionally, head and neck cancer (HNC) patients see a Speech-Language Pathologist (S-LP) after their treatment is completed to address any swallowing-related concerns (Govender, Smith, Gardner, Barratt, & Taylor, 2017). The question has been raised now about seeing an S-LP prior to treatment to preemptively address potential post-treatment-related dysphagia. The reasoning behind this is that if HNC patients undergoing non-surgical treatment are not actively and intentionally using their swallowing musculature, this may affect their ability to swallow efficiently and without causing harm to themselves after treatment. Prophylactic swallowing therapy has been seen as a potential way to address these issues regarding post-treatment swallowing function.

Those who incur chronic dysphagia after treatment report a severe negative effect on their quality of life (Michaelsen, Grønhøj, Michaelsen, Friborg, & Buchwald, 2017). Some of the effects are specific to eating, such as saliva production, chewing, and swallowing, and some of the effects are felt in other areas, such as physical appearance and emotional health. It is important then to understand how to best address and preserve swallowing function with patients in this population in order to preserve their quality of life and better their long-term outcomes.

Objectives

The primary objective of this review is to critically evaluate existing literature regarding the impact of prophylactic swallowing therapy on post-treatment dysphagia for HNC patients that will undergo chemoradiation and/or radiation therapy. The secondary objective is to provide recommendations for clinical practice and future research.

Methods

Search Strategy

Articles related to the topic of interest were found using the computerized database *PubMed* and Google Scholar. The initial search was (prophylactic swallowing therapy) AND (head and neck cancer) AND (chemoradiation OR radiation). This search yielded many articles, and further narrowing was required, which included AND (dysphagia) NOT (behavioural) NOT (quality of life) NOT (post-treatment)

Selection Criteria

Studies selected for inclusion in this critical review were required to investigate prophylactic swallowing therapy, head and neck cancer patients, chemoradiation and/or radiation therapy treatment, and dysphagia outcomes.

Data Collection

Results of this literature search yielded five articles congruent with the aforementioned selection criteria. Two of the studies employed a randomized control trial design, two were case control designs (one prospective and one retrospective), and one was a meta-analysis study.

Results

Randomized Control Trials (RCT)

Randomized control trials are an appropriate study design for looking at prophylactic swallowing

therapy programs' effect on dysphagia outcomes. An RCT is a type of study where a group of participants are randomly assigned to two or more intervention groups. One of these interventions is the control group. The results or outcomes are measured and compared across all groups. These types of studies are a very reliable way to test new treatment protocols. They can differ in their quality though, which can affect the strength of the study. The PEDro scale was used to evaluate the RCT's.

Kotz et al. (2012) completed a study that recruited 26 patients with a HNC diagnosis to study the effectiveness of a prophylactic swallowing exercise program on swallowing-related outcomes for patients undergoing chemoradiation therapy (CRT) in a prospective RCT study. Exclusion criteria were noted. A group of 13 participants were randomly assigned to the control group. They received the standard of care, which included referral to an S-LP following treatment if swallowing concerns arose. The other 13 participants were assigned to the intervention group. Five swallowing exercises were chosen for the intervention group based on their previously proven effectiveness. Three sets/ten repetitions a day for each exercise was the recommended dosage, and each participant saw an S-LP weekly to ensure compliance and correct usage of techniques. It was not disclosed how many weeks prior to and during CRT the patients performed these exercises.

Outcome measures included two appropriate swallowing-specific performance scales. A clinician trained in these scales and blinded to the intervention protocol assessed all 26 participants at one week, three-, six-, nine-, and 12-months after CRT. No other blinding was reported. All participants completed seven weeks of CRT, and all patients completed the follow-up. Of the 13 intervention patients, nine did not complete the protocol, with four dropping out after four weeks and five after five weeks. The participants reported discontinuing due to CRT effects, and not intervention effects.

Appropriate nonparametric statistical tests were used for patient comparison. Outcomes for both groups were examined in intention-to-treat analyses. Significantly higher functional swallowing and swallowing-related QOL scores were reported for the intervention group at the three- and six-month time points. The authors acknowledged limitations related to the small sample size. They also commented that statistically significant differences may be found at the nine- and 12-month time points if this study was trialed on a larger sample size.

Overall, this study provides suggestive evidence that a prophylactic swallowing exercise program improves swallowing outcomes in HNC patients following CRT. The randomized study design, a score of "8" on the PEDro scale, assessor blinding, weekly check-ins with an S-LP, and improved outcomes at multiple time points add to the strength of the study. However, the small sample size and lack of statistically significant differences in scores at the later time points leads to only a suggestive level of evidence.

Mortensen et al. (2015) conducted a study in Denmark examining a sample of 44 participants in a study designed to evaluate the impact of a prophylactic swallowing exercise program on swallowing-related outcomes for HNC patients treated with radiotherapy (RT). This prospective RCT study randomly assigned 22 patients to either the swallowing exercises or standard care group. Eligibility criteria were disclosed. Of the initial 44 patients, only 21 completed the study to 11 months, with 23 dropping out. Five patients withdrew due to a change in their treatment plans, 13 patients withdrew due to fatigue, and five patients had recurrence or died. Dropouts affected both randomization arms equally. The intervention group was instructed to perform all training exercises for three sets/ten repetitions a day. It was not disclosed how many weeks prior to and during CRT the patients performed these exercises. An experienced occupational therapist (the profession that undertakes dysphagia therapy in Denmark) saw the participants at nine different time points. These sessions focused on motivation and proper technique usage. The patients in the control group were given dietary advice and access to a Modified Barium Swallow Study (MBSS) as required. No blinding at any stage was reported.

The primary outcome measure was based on an appropriate statistical analytical global swallowing measure. MBS examinations were used to assess functional swallowing ability pre-treatment, and at two-, five-, and 11-months post-treatment completion. No statistically significant differences were found in the swallowing outcomes for either group at the check-in points. Clinically interesting results were that lower penetration, residue, and aspiration were found in the intervention group at two- and five-months post-treatment.

Overall, this study provides an equivocal level of evidence that a prophylactic swallowing exercise program improves swallowing outcomes in HNC patients following RT. The strength of this study was

its randomized design, the PEDro score of "6", and multiple outcome measures, including the objective MBS measure. There were many weaknesses though, including the high dropout rate, low adherence, which the authors acknowledged. This leads to an equivocal level of evidence in this study.

Case Control Studies

Case control study designs provide a weaker level of evidence when compared to an RCT study, but still provide an opportunity to compare two groups and their exposure to and outcomes from a common element. They are observational studies, which are an appropriate study design to look at prophylactic swallowing therapy programs' effect on dysphagia outcomes, but the clinical implications may be weaker due to the biases that can occur within this less-controlled study type.

A retrospective case-control study by **Carroll et al. (2008)** looked at the effects of a pre-treatment swallowing exercise program on post-treatment swallowing function for patients who had undergone chemoradiation therapy (CRT). A total of 18 patients were chosen, with nine patients in the pretreatment group, and nine in the control group. The pretreatment group received swallowing exercises to perform before CRT, and the control group received the standard care of post-treatment swallowing exercises as swallowing concerns arose. The intervention group began the swallowing exercises approximately two weeks prior to beginning CRT. The patients were instructed to perform the exercises for ten reps/five times daily. It was not reported if the exercises were taught by an S-LP, or if there was any follow-up to ensure the exercises were being done correctly. The length of CRT was not disclosed.

The outcome measures for this study were a Videofluoroscopic Study (VFS) examination completed approximately three months after treatment for both groups. A radiologist blinded to the study retrospectively scored the examinations. No other blinding was reported. Parameters and scales for scoring were disclosed. Despite the small sample size, parametrical statistics were completed. Results revealed that significant differences were found in three of the nine parameters scored on the VFS in favor of the intervention group.

Overall this study provides an equivocal level of evidence that a pre-treatment swallowing program affects the swallowing outcomes of HNC patients after completing CRT. Many elements of this study were not disclosed, making it hard to replicate, and the small sample size and low number of statistically significant differences in the outcome measures affect its strength and clinical implications. However, the blinded review of the objective VFS outcome measure allows this study to provide an interesting starting point for future research. These factors lead to an equivocal level of evidence.

Carmignani et al. (2018) conducted a prospective two-arm case control study that looked at the relationship between quality of life, vocal problems, and swallowing problems following CRT and/or RT in HNC patients. Only the effect on swallowing is of interest to the current review. A total of 60 patients were selected for this study, of which only 12 were included in the swallowing study. The control group included six participants, who all received the standard of care; diet modifications and medication. The other six participants were in the intervention group, and received a pre-treatment swallowing program prior to CRT/RT, as well as standard of care. Patients were randomly assigned to either group. No blinding was reported. Two weeks prior to commencement of CRT/RT, the intervention patients were instructed to perform swallowing exercises for ten reps/twice daily. The exercises were completed for eight weeks total; two weeks prior to treatment and six weeks during treatment. The swallowing exercises chosen were disclosed and were taught by a study author. It was not reported if there was follow-up to ensure correct performance of exercises.

Outcome measures included two valid and reliable self-administered swallowing-related questionnaires given two weeks prior to treatment, and again one-week and three-months post treatment. A mean compliance of 70% was reported.

A nonparametric multivariate analysis was completed on both questionnaire results at all three-time points. Results revealed statistically significant questionnaire answers from the control group at the one-month post-treatment time point. Weight and diet type trends worth noting from the multivariate analysis were that the control group had significantly higher weight loss, and the intervention group had a higher rate of solid food consumption. The authors acknowledged limitations of the study related to the small sample size, short longitudinal follow-up period, and lack of objective instrumental evaluation.

Overall, an equivocal level of evidence can be taken from this study. The lack of reported blinding, short follow-up period, small sample size, and only subjective outcome measures lead to this conclusion. There were statistically significant results at the 1-month post-treatment period in regards to

questionnaire results, but that is not enough to move this study beyond the rating of an equivocal amount of evidence that a prophylactic swallowing program is beneficial for swallowing-related outcomes in HNC patients receiving CRT/RT.

Meta-Analysis Study

A meta-analysis study is an effective way to analyze a variety of studies about an intervention in an objective way. This helps to provide clarity about the utility of an intervention, and what the conclusion of a body of studies was. This is an appropriate study design to use when considering the effectiveness of a prophylactic swallowing program on swallowing related outcomes for HNC patients undergoing CRT/RT.

A meta-analysis of studies related to the effects of a therapeutic swallowing exercise program undertaken before, during, and/or after CRT/RT for HNC patients was conducted by **Perry, Cotton, Kennedy, and Lee in 2016.** Search methods and dates were disclosed. Selection criteria were disclosed, including type of studies included, which were RCTs, and stages of cancer. The main comparison was between therapeutic exercises vs. treatment as usual. Six studies were included in the meta-analysis. Data was not pooled due to significant differences in interventions and outcomes evaluated. Lack of standardization was found regarding time points.

Primary outcomes were disclosed and were determined via appropriate objective measures. The GRADE system found the level of evidence for each study to be "very low". This was due to the small sample sizes and the quality of the study designs. No evidence was found that implementing a therapeutic swallowing program before, during, and/or after RT/CRT in HNC patient's leads to an improvement in their oral swallowing post-treatment. The authors acknowledged that this may be due to the small sample sizes in each study used, resulting in insufficient numbers to produce any statistically significant difference.

The findings of this study provide an equivocal level of evidence that there is a benefit to swallowing-related outcomes if a prophylactic swallowing treatment is implemented prior to CRT/RT for HNC patients. There was no statistically significant difference found between the intervention and control groups in the studies in swallowing-related outcomes.

Discussion

Overall, the findings from these studies suggest that there is only an equivocal level of evidence supporting the implementation of prophylactic swallowing therapy for HNC patients undergoing chemoradiation/radiation to improve their dysphagia outcomes. Four of the five studies provided an equivocal level of evidence, while one study provided a suggestive level of evidence. A common theme for the weaknesses of the studies were their small sample sizes, lack of consistent blinding, and short follow-up periods. Most authors acknowledged that if they had bigger sample sizes and a longer follow-up period, this might have changed the outcome of their studies in that more statistically significant differences may have been found in favour of the intervention group.

While the studies were all looking to answer the same question, the approach each took varied in many ways. For example, there were differences in sample sizes, follow-up time points, outcome measures, types of exercises implemented, and different guidelines for sets and repetitions for the exercises. While the variety in these approaches provided a range of data about this intervention option with the HNC population and its impact on post-treatment dysphagia, Perry et al (2016) argued the point that a more methodical and unified approach needs to be implemented in future research. Having standardized measurements and protocols that are consistently used across many studies will lead to a stronger evidence base for future meta-analyses. This could affect what direction the evidence points towards regarding the implementation of a prophylactic swallowing therapy program for reducing post-treatment dysphagia in the HNC population undergoing chemoradiation/ radiation in the future.

Conclusion

The studies viewed in this literature review provided an equivocal level of evidence in the support of implementing a prophylactic swallowing therapy program for reducing post-treatment dysphagia in HNC cancer patients undergoing radiation/ chemoradiation. The need for further research is apparent in this population group, as there were many weaknesses noted in the studies. Creating and implementing standardized measurements and protocols when conducting future studies with this scientific question in mind will lead to a stronger evidence base in the future.

Clinical Implications

The level of evidence provided by these studies was not strong, and it is unclear if this approach works with the HNC patient population. Therefore, clinicians should exercise caution when considering implementing this therapy approach. However, there were no negative effects reported by the patients after using a prophylactic swallowing therapy program. Clinicians should keep up to date on current research in this area to provide evidence-based care, as new research may provide statistically significant outcomes that may influence their practice when working with HNC patients undergoing chemo/radiation and the reduction of treatment-related dysphagia.

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