Original Article

Investigation of the Effect of Subglottic Aspiration on the Development of Ventilator-Related Pneumonia in Entubed Patients: A Systematic Review

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Abstract

Objectives: This systematic review explores the use of subglottic suction (SC) ports impact on reducing ventilator- associated pneumonia (VAP).
Research Methodology: Studies were determined by scanning the Pubmed, Google Scholar, Science Direct, Cochrane and Medline databases, using keywords. As a result, thirteen studies were found which conformed to the inclusion criteria.
Findings: It was seen that in ten of the 13 studies, SG aspiration achieved a significant reduction in VAP rates. However, no significant results were found relating to SG aspiration and the length of stay in intensive care, the time spent attached to a mechanical ventilator, or mortality rates. SG aspiration characteristics in two studies were an aspiration duration of 8 and 15 seconds; in four studies, the lowest pressure was 20 mmHg and the highest was 100-150 mmHg. In no study were the complications of SG aspiration examined. Among methods used to prevent VAP were mouth care in five studies, patient head height in 11 studies, and a cuff pressure of 20-30 cmHg in ten studies.
Conclusion: In patients attached to a mechanical ventilator, entubation with catheters with subglottic aspiration achieved a reduction in the rate of VAP compared with classical intubation tubes. However, very few studies have examined both the characteristics of SG aspiration and other methods used to prevent VAP.

Keywords: Intubated, pneumonia, subglottic aspiration, VAP.

Introduction

Ventilator-associated pneumonia (VAP) is a widespread nosocomial infection in patients who need mechanical ventilation (Vincent et al., 2009). Between 9 and 35.4% of patients on mechanical ventilator support develop VAP (Othman and Abdelazim, 2017). With VAP, an extended stay in intensive care and in hospital increases the use of antibiotics and raises heath costs (Chawla, 2008). The VAP-related mortality rate varies between 9 and 76% (Elliott et al., 2015). VAP is defined by the European Centers for Disease Control and Prevention as pneumonia developing 48 hours or more after mechanical ventilator support (ECDC, 2010). The pathology of VAP is multi-factorial, but it mostly derives from micro-organisms colonizing the oropharynx or aspiration of gastric content (ATS, 2005). An endotracheal tube interferes with the normal protective reflexes of the upper airway, reduces effective coughing, causes irritation of the respiratory mucosa, increases the amount of mucus, and increases micro-aspiration of contaminated oropharyngeal secretions (Augustyn, 2007).

In the literature, the risk factors for VAP are stated to be inadequate mouth care, reduction in consciousness, body position, the presence of a naso-gastric tube, vomiting, swallowing dysfunction, the use of a ventilator and the insertion of an endotracheal tube, humidifier contamination, the use of antacids or H2 blocker drugs, and disregard of infection control protocols by care providers (Chastre and Fagon, 2002;Kollef et al., 1999). It has been shown that the re-use after a single use of a nebulizer adding drugs to the tube of the inspiratory phase of the mechanical ventilator (aerosol treatment) may be responsible for the bacterial colonies (Craven et al., 1984). There are also related factors such as neurosurgery or neurological damage, thoracic or upper abdominal surgery, a poor state of health, a history of lung disease, diabetes mellitus and length of stay in hospital (Chastre and Fagon, 2002).

Both pharmacological and non-pharmacological methods can be used in the control of VEP infection. Pharmacological methods include chlorhexidine solution (Munro and Grap, 2004) and also c-globin (Kollef et al., 1999). Among non-pharmacological methods are using the nose rather than the mouth as a route of intubation (Bert and Lambert, 1996), comprehensive oral care (Garcia, 2005), continuous subglottic aspiration (Smulders et al., 2002), hand washing (Nagata et al., 2002), height of the bed head to avoid excessive load on the stomach (Torres et al., 1992), preserving normal stomach pH, selective digestive decontamination and aspiration of subglottic secretions (Ahrens et al., 2004; Hess, 2005; Kalil et al., 2016). Micro-aspiration mostly occurs when the intubation cuff is at low pressure (Blunt, 2001). The semi-recumbent position reduces the risk of VAP compared to the supine position by reducing micro-aspiration(Alexiou et al., 2009;Orozco et al., 2005). Cleaning the oropharynx with chlorhexidine reduces the risk of VAP by achieving a reduction of bacterial colonies (Ahrens et al., 2004). Traditional tubes only allow the intermittent removal of intraluminal secretions without having any effect on subglottic secretions, whereas the new tubes allow the continuous aspiration of subglottic secretions (Mahmoodpoor et al., 2017). It was reported in a study by Lacherade (2010) that a reduction in pharyngeal colonization was achieved in patients given SG aspiration. It was shown radiographically that before secretions entered the lower respiratory tract as micro-aspiration, they collected above the cuff of endotracheal tubes, in the subglottic region. Subglottic aspiration and the cuff inside the endotracheal tube are intended to prevent the advance of bacterial colonies accumulating on the lumen into the lower respiratory tract (Huang et al., 2018). With this aim, an external lumen was added in the design of the intubation tube, allowing the intermittent or continuous removal of subglottic secretions (Dezfulian et al., 2005). Aspiration of subglottic secretions is one of the widely used methods used to prevent VAP. In a study conducted in hospitals in the United States of America, it was found that intubation tubes which provided SG aspiration were routinely used with 55% of patients (Krein et al., 2015). Guides in the USA, Canada and Australia recommend subglottic aspiration (Klompas et al., 2014; Lerma et al., 2014).

However, VAP has multifactorial origins, and no single intervention can by itself have a decisive effect on it. It is recommended that a combination of measures be used: oral care, tooth brushing, cuff pressure, patient position, monitoring gastric residue, and subglottic aspiration. Systematic and meta analyses examining the effectiveness of subglottic aspiration in preventing VAP have not adequately considered other methods. Therefore, the first question of our systematic review was to examine whether subglottic aspiration was more effective in alleviating the risk of VAP when used together with other preventative measures. The second question of the study was to examine the features (method, frequency and duration of aspiration) and complications (drying and the risk of trauma) of subglottic aspiration and the development of VAP, length of stay in intensive care, duration of attachment to a mechanical ventilator, and mortality rates. Many systematic reviews and meta analyses have examined the effects of subglottic aspiration on VAP prevention, duration of stay in intensive care, duration of attachment to a mechanical ventilator and health expenditure. The features of subglottic aspiration and other preventative methods used are inadequate. This is because the levels of

proof of the studies are inadequate. Because of this limitation of previous systematic reviews, in this study we investigate the effect on the prevention of VAP with regard to certain variables of subglottic aspiration by examining these variables, which have an effect on the development of VAP.

Material and Method

Study description/protocol: In this systematic review, it was reported that subglottic aspiration in intubated patients conformed with PRISMA operation steps of studies which included the prevention of VAP.

Criteria for inclusion in the study

The criteria for the study's inclusion are defined according to PICOS. **P- Population:** Patients aged 18 and over are connected to mechanical ventilators for at least 48 hours. **I- İnterventions:** Subglotis aspiration application. **C- Comparisons:** Subglotis aspiration is not applied or applied differently from the application group. **O- Outcomes:** VAP diagnostic criteria, time to stay in mechanical ventilator, mortality. **S: Study designs:** Randomized controlled, controlled clinical and semi-experimental research.

Exclusion criteria

Studies with patients who had undergone a surgical operation or trauma, an impairment of the upper respiratory tract, a chronic respiratory tract disease, a lung infection or a tracheostomy, or who were receiving chemotherapy or radiotherapy treatment were excluded from the research. Furthermore, studies that have not been fully texted and non-English language.

Selection of studies

Research data was accessed using the Pubmed, Science Direct, Cochrane, Medline and Google Scholar databases. These were scanned with the key words intubated, subglottic aspiration, pneumonia and VAP which conformed to MESH. Research articles published in accordance with the research protocol between 1992 and March 2020 and whose full text was accessible were included in the study. The last time the screening was done was on March 15.

Data extraction

Data extraction from the studies determined in accordance with the research protocol which had been created was conducted by two researchers independently. Data was collected from each study on frequency, duration and method of subglottic aspiration, frequency of oral care, tooth brushing, solution used in oral care, cuff pressure, patient position, gastric residue monitoring, VAP diagnosis, length of stay in intensive care, duration of attachment to mechanical ventilation, APACHE II score, use of antibiotics, mortality rate, number of patients, publication year, patients' characteristics, and results. In order to assess the quality of research, it was evaluated by two writers using the Jadad score and the Newcastle Ottawa standard. The validity of the Jadad scale has been approved, and it assesses the quality of randomized double-blind studies. The Jadad score varies from 0 to 5. A Jadad score of <2 shows that a study is of low quality, while a score of 2 or more denotes a high quality study. The Newcastle Ottawa scale assesses the quality of cohort studies and case studies. Scoring on the scale is calculated between 0 and 9.

PRISMA Flow diagram (Liberati et al., 2009)

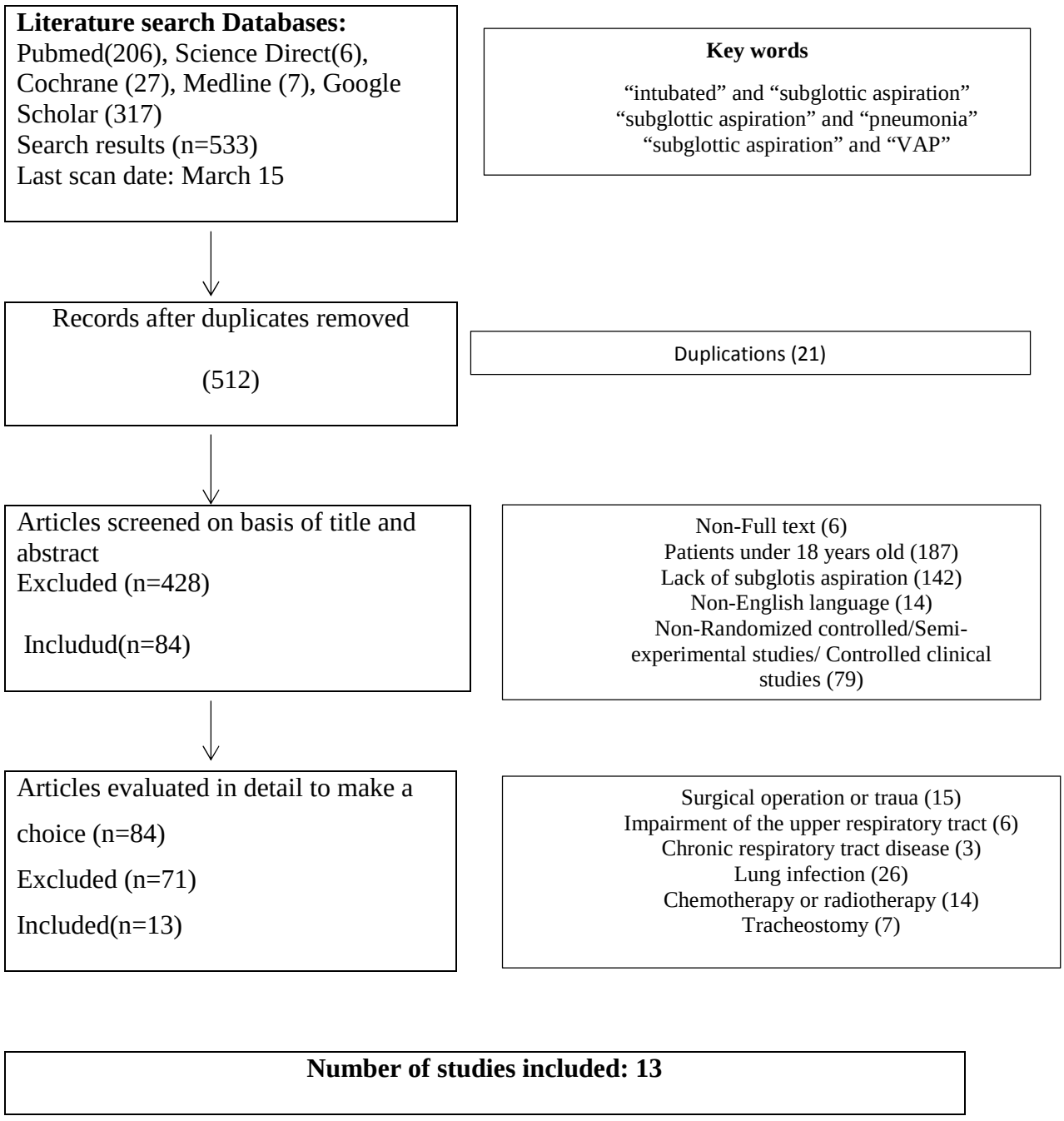

Fig. 1 Flow diagram describing process of articles being reviewed and selected

Section/topic	#	Checklist item	Reported on page #
ITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3,4,5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6,7,8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6,7,8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6,7,8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6,7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6,7,8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	14,15,16,17

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6,7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	------
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	14,15,16,17
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	-------

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-----
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	------
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7,8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	16,17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	------
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11, 12, 13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	------
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	-----
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-----

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	-----
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	-----

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Results

General findings on the studies: The studies included in the research were conducted between 1992 and 2018 in the USA, France, Iran, Japan, Turkey, the Netherlands, Poland, Spain, India and Belgium. Duration of intubation of included patients was at least 48 hours in ten studies, and at least 72 hours in four studies. Mean age groups of patients in the included studies were 50-60 in five studies and 61-71 in eight studies. Regarding mean APACHE II scores among the patients in the studies, in three studies there was a difference between means, in six studies there was not, and in four studies it was not examined (Table 1).

Subglottic aspiration characteristics: Subglottic aspiration frequency was continuous in one study, every 20 seconds in two studies, every hour in three studies, every two hours in three studies, every six hours in one study, automatic in one study, and not specified in two studies. The method of aspiration was with the intubation tube which was the subglottic aspiration lumen and with a 10cc syringe in two studies, with the intubation tube which was the subglottic aspiration lumen and with a continuous aspiration device in three studies, and with the intubation tube which was the subglottic aspiration lumen and an intermittent aspiration device in eight studies. The duration of aspiration was not specified in only two studies; otherwise, it was given as 8 seconds, 15 seconds or less. Aspiration pressures were given as 100 and 100-150 mmHg in two studies where intermittent aspiration was used, and as 20 and 30 mmHg in two studies where continuous aspiration was used (Table 1).

Other methods used to prevent VAP: In only two studies, chlorhexidine was used in oral care, and povidone iodine was used in one study. Frequency of oral care was given as once a day in one study, six times every four hours in one study, four times every six hours in one study, and three times every eight hours in two studies. In only one study, it was stated that tooth brushing was performed in oral care. Patients' positions were changed every two hours in three studies, every three hours in one study, every four hours in three studies, and every 12 hours in one study. In most of the studies, patients' heads were kept raised at an angle of 30-45°. In ten studies, cuff pressure was 20-30 cmHg (Table 1).

Patient outcomes: In 12 of the studies, subglottic aspiration was performed on an intervention group, but not on a control group. According to the conclusion of this study, VAP rates were found in nine studies to be significantly lower in the intervention group than in the group in which subglottic aspiration was not performed, while no significant difference was found in three studies. It was reported in only two studies that subglottic aspiration reduced the length of stay in intensive care, and in only two studies was a reduction in duration of attachment to MV observed in comparison with the control group. It was stated in all studies that subglottic aspiration did not reduce mortality rates (Table 2).

In only one of the studies, continuous subglottic aspiration was performed with patients of the intervention group, while intermittent subglottic aspiration was performed with the patients in the control group. According to the results of that study, a reduction in the rate of VAP was seen with continuous as opposed to intermittent subglottic aspiration, while intermittent aspiration was found to reduce the length of stay in intensive care or on a mechanical ventilator. No significant difference was found in mortality rates (Table 2).

Quality assessment: Eleven of the 14 studies included in the research were randomized controlled studies. The Jadad quality scores were 3 for three studies, 4 for three studies, 4.5 for two studies, and 5 for two studies. The Newcastle Ottawa scores of the studies which were not randomized controlled studies were 2 for one study and 4 for one study (Table 2).

Discussion

The aim of this systematic study was to review studies on the effectiveness of subglottic aspiration in preventing pneumonia. A large number of systematic reviews and meta analyses on this topic have been conducted. The difference between our study and these sources is that in the studies included in the review, the differences between various subglottic aspiration implementations are determined. Our study at the same time examined variables relating to the ventilator – mouth care, chlorhexidine use, cuff pressure, patient position –

used in the prevention of pneumonia. In this way, it was investigated whether other variables that may be effective in the development of pneumonia are also involved in the studies. This information is necessary for the homogeneity of studies. Homogeneity of studies will increase the reliability and generality of the results. Heterogeneity of the study will cause the information obtained to be limited. When the studies included in our research were examined for the frequency of subglottic aspiration, only two performed continuous aspiration, and in the others aspiration was intermittent, with the smallest interval of 20 seconds, and the greatest of six hours (Sole and Bennet, 2011;Sole et al., 2003). The volume of mouth secretion was found to be greatest (7.5ml) with aspiration at an interval of four hours, and in some patients this volume was as much as 25ml (Sole and Bennet, 2011). Studies have found that both continuous and intermittent aspiration are effective in preventing VAP, and that the intervals do not show a statistical difference (Dezfulian et al., 2005; Fujimoto et al., 2018;Smulders et al., 2002). However, it is reported in some studies that patients in whom continuous subglottic aspiration is implemented are susceptible to tracheal trauma and edema (Berra et al., 2004;Girou et al., 2004;Lacherade et al., 2018; Seguin et al., 2018). None of the studies included examined the complications of SG aspiration. It is recommended in a study by Mahmoodpoor et al. (2017) that in order for continuous aspiration not to cause tracheal trauma, subglottic aspiration should be performed at six hourly intervals. It is reported in the literature that subglottic aspiration makes patients, especially those with low saliva production and those with dryness of the mouth, more prone to tracheal trauma, and causes edema (Dragoumanis et al., 2007;Jaensson et al., 2010;Santos et al., 1994;Suysa et al., 2013). The duration and pressure of subglottic aspiration as risk factors for trauma of the trachea are mentioned in only two studies.Examining the studies included in our research for non-pharmacological methods used in the prevention of VAP, it was found that oral care was performed in only four of the studies.

There were differences in the frequency of oral care, the solution used, and in tooth brushing. In many studies in the literature, comprehensive oral care and chlorhexidine secured a reduction in VAP rates. Also, the importance of oral care in the prevention of VAP is emphasized in guides and evidence-based implementations (Garcia, 2005;Siobal et al., 2001). It is reported that subglottic aspiration is effective in the prevention of VAP, but that when it is used in conjunction with a semi-recumbent position and comprehensive oral care, it secures a much greater reduction in rates of VAP (Mao et al., 2016;Van et al., 2006). A semi-recumbent position with the head at an angle of 30 degrees or more reduces VAP, and this practice is a part of the routine care protocol in intensive care (ATSIDSA, 2005;Cameron et al., 1973). In most of the studies included in our research, it is stated that the semi-recumbent position was used in the VAP prevention care protocols.Examining the cuff pressure used in the prevention of VAP in the studies included in our research, it was found to be between 20 and 30 cm Hg in most of them. In the literature, it is recommended that cuff pressure should be checked at 12 hourly intervals, and kept at a pressure of 20-30 cm Hg (Alvarez et al., 2014;Bernhardt and Cottrell, 1975; Sole et al., 2019). Guides emphasize the importance of cuff pressure in the prevention of VAP, and make recommendations, but there are no recommendations on the frequency of cuff pressure (ATSIDSA, 2005;Alvarez et al., 2014). According to one study, a reduction in the rate of VAP was seen when subglottic aspiration and continuous cuff pressure were implemented together (Tablan et al., 2004).In most of the studies, VAP rates in groups given subglottic aspiration were significantly lower than in patient groups to whom it was not given. Systematic reviews and meta analyses showed similar findings (Carrascosa et al., 2020;Wang et al., 2015). However, the difference between VAP rates was found to be large. It can be said that patient characteristics, sample size, other preventative measures (semi-recumbent position, frequency of oral care, tooth brushing and chlorhexidine use) or characteristics of subglottic aspiration may have caused this difference in VAP rates.

Tablo 1. Subglottic aspiration characteristic and variables

Year, country, writer	Mean age	Subglottic aspiration frequency	Oral care frequency and solution	Tooth brushing	Patient position	Cuff pressure	Nasogastric residue monitoring	APACHE II score
2010 France; Lacherade JC, Jonghe BD, Guezennec P, Debbat K, Hayon J, Monsel A,	Int: 67 Cntrl: 70	Manually every hour	-------- --------	----------	Semi Fowler position, 3 hourly check	20-30 cmHg 3 hourly check	Int: 90 Cntrl: 87	----------
2017 Iran, Mahmoodpoor A, Hamishehkar H, Hamidi M, Shadvar K, et al.	Int: 54 Cntrl: 54	6 hourly	---------- Chlorhexidine	----------	Head elevation 45^0	20-30 cmHg 6 hourly check	----------	Int:22.6 Cntrl: 21.4 Difference found between group mean scores
2011 India, Juneja D, Javeri Y, Singh O, Nasa P, et.al.	Int: 54.5 Cntrl: 52	Intermittent, automatic	---------- Chlorhexidine	----------	Head elevation 30-45^0	20-30 cmHg 24 hourly check	----------	Int: 24.5 Cntrl: 22.7 No difference found between group mean scores
2018, Japan Fujimoto H, Yamaguchi O, Hayami H, Shimosaka M, Tsuboi S, Sato M	Int: 68.1 Cntrl: 70.9	At 20 second intervals At 2 hour intervals	8 saat aralıklı Povidone iodine	----------	Head elevation 45^0 2 hourly check	20 cmHg 2 hourly check	----------	Int: 14.6±5.7 Cntrl: 14.8±3.8 No difference found between group mean scores
1992 France, Auboyer MC, Jospe R, Ros A, Guerin C, Khouri Z, Galliez M, Dumont A	57 and above	Aspiration every hour with 10cc syringe	------ -------	----------	----------	30 cmHg 8 hourly check	---------	----------

2018 Turkey, Erinc A, Ozcelik HK, Yigitbas BA, Yurt S, Kosar F	Int: 64 Cntrl: 71	Every 2 hours	-------- -------- 	----------	Head elevation 30-45^0	----------	----------	Int: 17 Cntrl: 22.7 Difference found between group score means
2002 Netherlands, Smulders K, Hoeven H, Weers I, Grauls CV	Int: 63.7 Cntrl: 62.8	Every 20 seconds	--------- ---------- 	----------	---------- Position change every 4 hours	----------	----------	Int: 21.3 Cntrl: 22.3 No difference found between group mean scores
1999 USA, Kollef MH, Skubas NJ, Sundt TM	Int: 64.7 Cntrl: 62.5	Continuously every 20 seconds	---------- ---------- 	----------	----------	----------	-------	Int: 11.1 Cntrl: 11 No difference found between group mean scores
2017 Poland, Walaszeka M, Gniadekb A, Kolpac M, Wolakc Z, Kosiarskac A	Int: 59 Cntrl: 56	----------	---------- ---------- 	----------	----------	20-30 cmHg	----------	---------
2014 Spain, Lorente L, Lecuona M, Jiménez A Cabrera J, Mora ML.	Int: 60 Cntrl: 62	Every hour	Every 8 hours -%0.12 Chlorhexidine	----------	Head elevation 40 ^{0} 4 hourly check	25 cmHg 8 hourly check	Gastric residue check every 6 hours. >250 ml taken as normal.	Int: 17.01 Control: 13.92 No difference found between group mean scores
2008 Spain, Bouza E, Pérez MJ, Mun P, Rincón R, Barrio JM, Hortal J.	Int: 65.7 Cntrl: 65	Continuous	--------- --------- 	----------	----------	20-30 cmHg	--------	Int: 10.2 Cntrl: 10.4 No difference found between group mean scores
2016 India, Vijai MN, Ravi PR, Setlur R,	Int: 56.12 Cntrl: 57.22	Every 2 hours	---------- ---------- 	----------	---------- 4 hourly check	20-30 cmHg 4 hourly check	----------	Int: 16.42 Cntrl: 19.02 Difference found between group

Vardhan H.								mean scores
2015 Belgium, Damas P, Frippiat F, Ancion A, Canivet J-L, Lambermont B, Layios N,	Int: 66 Cntrl: 65	----------	---------- Chlorhexidine	Yes	Head elevation 30^0	20-30 cmHg	----------	----------

Table 2. Subglottic aspiration and patient outcomes

Year, country, writer	Intervention group	Control group	Research design	Sample size	Pneumonia development N (%)	Mean stay in intensive care (days)	Mean attachment to MV (days)	Mortality	Jadad score	Newcastle - Ottawa
2010 France; Lacherade JC, Jonghe BD, Guezennec P, Debbat K, et al.	Each hour, subglottic secretion, manually with a 10 cc syringe	Subglottic aspiration not performed.	4 different centers, Randomized controlled clinical experimental study	Int: 169 Cntrl: 164 At least 48 hours connected to MV	Int: 25 (14.8) Cntrl: 42 (25.6) **p<0.05**	Int: 8 Cntrl: 8 **p>0.05**	Int: 11 Cntrl: 11 **p>0.05**	Int: 71 (42.0) Cntrl: 65 (39.6) **p>0.05**	+5	
2017 Iran; Mahmoodpoor A, Hamishehkar H, Hamidi M, Shadvar K, et al.	Every 6 hours, subglottic aspiration at 100 mmHg pressure for 15 seconds at most	Subglottic aspiration not performed.	Randomized controlled clinical experimental study	Int:138 Cntrl:138 At least 72 hours connected to MV	Int:30 (21.7) Cntrl:46 (33.3) **p<0.05**	Int:15 Cntrl: 18 **p>0.05**	Int:11.6 Cntrl: 12.3 **p>0.05**	Int: 36 (27.3) Cntrl: 48 (37.2) **p>0.05**	+4,5	
2011 India, Juneja D, Javeri Y, Singh O, Nasa P, Pandey R, et al.	Intermittent automatic subglottic aspiration	Subglottic aspiration not performed.	Single centered controlled study	Int: 60 Control: 78 Connected to MV for 72 hours or more	Int: 5(8.3) Control:11(14.1) **p<0.05**	Int: 8.4 Control: 7.8 **p>0.05**	Int: 10.9 Control: 10.4 **p>0.05**	Int: 16 (26.7) Control: 23 (29.5) **p>0.05**		+2
2018, Japan Fujimoto H, Yamaguchi O, Hayami H, Shimosaka M, Tsuboi S,	Continuous subglottic aspiration at 30cmH_2O pressure	2 hourly subglottic aspiration at 100-150 mmHg pressure	Single centered randomized controlled experimental study	Int: 15 Cntrl:16 At least 48 hours connected to MV	Int: 4 (26.7) Control: 7 (43.8) **p<0.05**	Int: 6 Cntrl:9 **p<0.05** Continuous subglottic aspiration	Int: 3.7 Cntrl: 6.9 **p<0.05** Continuous subglottic aspiration	Int: 2 (13.3) Cntrl: 2 (12.5) **p>0.05**	+3	

1992 France, Auboyer MC, Jospe R, Ros A, Guerin C, et.al.	Hourly subglottic aspiration	Subglottic aspiration not performed.	Single blind randomized controlled study	Int: 70 Cntrl:75 Connected to MV for 72 hours or more	Int: 9(12.8) Cntrl:21(29.1) **p<0.05**	Int:21.5 Cntrl:5.9 **p<0.001**	----------	Int: 33 (22.8) Cntrl: 47 (17.4) **p>0.05**	+4,5	
2018 Turkey, Erinc A, Ozcelik HK, Yigitbas BA, Yurt S, Kosar F.	2 hourly subglottic aspiration	Subglottic aspiration not performed.	Prospective randomized controlled study	Int: 12 Cntrl:30 At least 48 hours connected to MV	Int: 4 (33.3) Cntrl: 11 (36.7) **p>0.05**	Int: 15.5 Control: 18 **p>0.05**	Int: 11 Control: 15.9 **p>0.05**	Int: 5 (41) Cntrl: 21 (70) **p>0.05**	+3	
2002 Netherlands, Smulders K, Hoeven H, Weers-Pothoff I, Vandenbroucke-Grauls C.	Subglottic aspiration for 8 seconds every 20 seconds	Subglottic aspiration not performed.	Randomized controlled study	Int: 49 Cntrl: 56 Connected to MV for 72 hours or more	Int: 2 (4.1) Cntrl: 10 (17.9) **p<0.05**	Int: 11.9 Cntrl: 14.2 **p>0.05**	Int: 7.9 Cntrl: 7.1 **p>0.05**	Int: 9 (18.3) Cntrl: 10 (17.8) **p>0.05**	+4	
1999 USA, Kollef MH, Skubas NJ, Sundt TM.	Continuous subglottic aspiration at max. 20 cmHg pressure	Subglottic aspiration not performed.	Randomized controlled double blind experimental study	Int: 160 Cntrl: 183 At least 48 hours connected to MV	Int: 8 (5) Cntrl: 15 (8.2) **p>0.05**	Int: 3.7 Cntrl: 3.2 **p>0.05**	Int: 1.5 Cntrl: 1.9 **p>0.05**	Int: 6 (3.8) Cntrl: 8 (4.4) **p>0.05**	+5	
2017 Poland, Walaszek M, Gniadekb A, Kolpac M, Wolakc Z, Kosiarskac A.	Subglottic aspiration	Subglottic aspiration not performed.	Retrospective cross-sectional study with control group.	Int:1003 Cntrl: 804 At least 48 hours connected to MV	Uy: 43 (4.3) Cntrl: 86(10.7) **p<0.001**	Int: 6.8 Cntrl: 9.4 **p>0.05**	Int: 4.7 Cntrl: 5.6 **p>0.05**	Int: 16 (1.5) Cntrl: 29 (3.6) **p>0.05**		+4
2014 Spain, Lorente L, Lecuona M,	Hourly subglottic aspiration, manually with 10 cc syringe	Subglottic aspiration not performed.	Prospective, randomized controlled	Int: 84 Cntrl: 241	Int:17 Cntrl: 26	Int: 28 Cntrl: 49	Int: 13.56 Cntrl: 5.23	----------	+3	

Jiménez A Cabrera J, Mora ML.			observational study	At least 48 hours connected to MV	**p<0.05**	**p<0.05**	**p<0.05**			
2008 Spain, Bouza E, Pérez MJ, Mun P, Rincón R, et al.	Continuous subglottic aspiration at 100-150mmHg pressure	Subglottic aspiration not performed.	Randomized controlled study	Int: 331 Cntrl: 359 At least 48 hours connected to MV	Int: 12 (3.6) Cntrl: 19 (5.3) **p>0.05**	Int: 3 Cntrl: 3 **p>0.05**	Int: 17.9 Cntrl: 27.6 **p>0.05**	Int: 23 (6.9) Cntrl: 26 (7.2) **p>0.05**	+3	
2016 India, Vijai MN, Ravi PR, Setlur R, Vardhan H.	2 hourly manual subglottic aspiration with a 10 ml syringe	Subglottic aspiration not performed.	Randomized controlled study	Int: 54 Cntrl: 56 At least 48 hours connected to MV	Int: 3 (6) Cntrl:11 (22) **p<0.05**	Int: 11.3 Cntrl: 14.4 **p>0.05**	Int: 8 Cntrl: 6.45 **p<0.01**	Int: 18 (36) Cntrl: 24 (48) **p>0.05**	+4	
2015 Belgium, Damas P, Frippiat F, Ancion A, CanivetJ-L, LambermontB, Layios N, et al.	Subglottic aspiration	Subglottic aspiration not performed.	Randomized controlled study	Int: 170 Cntrl: 182 At least 48 hours connected to MV	Int: 15 (8.8) Cntrl: 32 (17.6) **p<0.05**	Int: 19 Cntrl: 12 **p>0.05**	---------- **p>0.05**	Int: 78 (45.9) Cntrl: 93 (51.1) **p>0.05**	+4	

The effect of subglottic aspiration on duration of attachment to MV was found to be significant in only one study. The reason for this may be that the patient groups included were followed up for a long time. Although the application of subglottic aspiration in the early stages is reported to be effective in preventing VAP, only two of the studies examined the effects of subglottic aspiration in early stage intubation (5 days or less). In the USA, Canada and part of Europe, national guides recommend subglottic aspiration to prevent VAP only in the early stages (in the first five days of intubation, Alvarez et al., 2014; Muscedere et al., 2008). This is supported in the literature (Mao et al., 2016; Wang et al., 2015;Vijai et al., 2016). In many studies and meta analyses, this effect of subglottic aspiration is not emphasized.The mortality risk in patients who develop VAP is 5-9% higher than in those who do not develop VAP (Bekaert et al., 2011; Melsen et al., 2011). In none of the studies included in our research was subglottic aspiration observed to reduce mortality rates. There are also studies in the literature which report that subglottic aspiration reduces mortality rates or that it has no effect (Carrascosa et al., 2020;Mao et al., 2016; Wang et al., 2015).

The Jadad scores of the randomized controlled studies were at a good level of 3-5, but the Newcastle Ottawa scores of the non-random studies were at a low level of 2-4. According to these quality measures, the studies showed a difference methodologically.

Implications for clinical practice: Subglottic aspiration system can be used to reduce VAP rates.

- In studies, subglottik can improve the reliability of research results by identifying variables that may affect aspiration results.
- Using subglottic aspiration with other VAP preventive methods may increase the effectiveness of the application.

Limitations of the study

The quality and reliability of the evidence obtained from the study findings was negatively affected by the fact that not all of the studies were randomized controlled studies, that they obtained low scores on the Newcastle Ottawa evaluation scale, that the study groups were heterogeneous, that the applications were different, and that possible complications of subglottic aspiration were not mentioned.

Conclusion and Recommendations

Intubation with catheters which have the capacity for subglottic aspiration not only lowers VAP rates in comparison with classic intubation tubes in patients attached to mechanical ventilators, it also has advantages such as reducing the time spent attached to the mechanical ventilator. However, along with the advantages of subglottic aspiration, there are various limitations to its use. There are insufficient studies of complications relating to subglottic aspiration. Also, other methods to prevent VAP which could affect the effectiveness of subglottic aspiration are little considered. It is recommended that these deficiencies should be considered in later studies.

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