Clindamycin use in head and neck surgery elevates the rate of infections in tracheostomies

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Received: 26 October 2021 / Accepted: 8 March 2022 / Published online: 25 March 2022 © The Author(s) 2022

Abstract
Background Surgical site infection (SSI) in open surgical tracheostomy (ST) occurs in up to 33% of the cases. SSI can be reduced by a postoperative antibiotic prophylaxis (POAP). The effect of Clindamycin on SSIs in head and neck surgery (HNS) is discussed controversially in the literature.

Methods An 8 year single-center retrospective comparative analysis of 441 STs (Visor-ST and Bjoerk-flap technique) performed within major HNS was evaluated due to the event of a SSI within 7 days and analyzed descriptively. Logistic regression model evaluated the impact of POAP with Clindamycin on SSIs.

Results The use of Clindamycin showed twice the rate of ST-SSI as all patients that did not receive Clindamycin, treated with other perioperative antibiotics. (Fisher’s \( p = 0.008 \)) The logistic regression model could not prove a statistically significant impact. (OR = 2.91, \( p = 0.04 \)).

Conclusion We recommend that Clindamycin should be reconsidered as a POAP regimen in ST. Further studies should evaluate alternatives for Penicillin-allergic patients.

Level of evidence III Comparative retrospective monocentric study.

Keywords Tracheostomy · SSI · Surgical wound infection · Antibiotic prophylaxis · Clindamycin

Introduction
The human and financial costs of treating surgical site infections (SSIs) are increasing [1]. A SSI is an infection originating in surgical wounds or the organs manipulated during an operative procedure, and is seen as the most common postoperative complication [2]. SSI occur within 30 days after the operation and consist of purulent drainage, organism growth from an aseptically won fluid or tissue, surgical wound exploration with no or a positive culture, or when a surgeon diagnoses a incisional wound infection [3].

The CDC classifies wounds according to the likelihood and degree of wound contamination during the operation. Therefore, wounds can be “clean”, where the respiratory, alimentary, genital, or uninfected urinary tract are not entered. “Clean-contaminated” wounds are operative wounds where the respiratory, alimentary, genital, or urinary tract is entered without unusual contamination. Most head and neck oncologic operations (HNOS) are counted to the group of “clean-contaminated” surgical wounds. Further, major breaks in sterile technique and incisions in which acute non-purulent inflammation is encountered, is classified as “contaminated wounds”, whereas “dirty or infected wounds” include necrotic wounds or perforated viscera. This last definition suggests that the organisms causing postoperative infection were present in the operative field before the operation [3].

The risk of establishing a SSI after head and neck surgery (HNS) ranges between a prevalence 0.37% [4], 20% [5] and 64% [6]. Lotfi et al. identified major risk factors
for establishing a SSI undergoing HNOS as advanced stage cancer, smoking, comorbidities, the need of major reconstruction of the surgical wound, and the submission of an inadequate perioperative antibiotic prophylaxis (POAP) [7]. The use of POAP in clean-contaminated HNOS is seen as mandatory to reduce the risk of SSI. [6, 8–11] Successful POAP requires effect against gram-positive, gram-negative, and anaerobic organisms [12]. The highest prevention rate of HNS-SSI were found for Cefazolin, Amoxicillin-Clavulanate and Ampicillin-Sulbactam [6]. Further, Piperacillin-Tazobactam is a good choice of treatment as monotherapy for SSI after HNOS [13].

Within many HNOS, surgical tracheostomy (ST) remains the favorable technique to permanently or temporarily secure the airway [14]. Wound infection in open, elective ST is caused by the bacterial flora of the skin and occurs in up to 33% of the cases [15, 16]. This minor local infection may spread and can cause serious complications like tracheitis, mediastinitis, clavicular osteonecrosis and necrotizing fasciitis [17]. In ST and even in percutaneous dilatational tracheotomy, perioperative antimicrobial treatment showed a reduction of SSI [9, 18].

Studies identified Clindamycin use in postoperative clean-contaminated HNS as a risk factor for establishing a wound infection, whereas extended duration of antibiotics was found not to be associated with an increased risk of postoperative infection [6, 10, 12, 19]. Therefore, the choice of antibiotics seems to be more important than the duration of HNS POAP [20].

We concentrated on the evaluation of SSI after ST and tried to quantify the risk of wound infection in patients receiving Clindamycin compared with patients who received other antibiotics or none.

Materials and methods

The work has been reported in line with the STROCSS criteria [21]. The trial has been registered under “Perioperative antimicrobial prophylaxis with Clindamycin elevates the rate of surgical site infections in tracheostomies? Findings in a retrospective comparative study in clean-contaminated head and neck surgery”, with researchregistry.com under “researchregistry7103”.

Institutional review board review and data protection

The study is stated as exempt due to IRB approval and EU data protection regulations. Our retrospective chart review fits the exempt criteria. The research involves the collection of existing data, documents, records, pathological specimens or diagnostic specimens and the data is recorded in an anonymous manner such that subjects cannot be identified directly or through identifiers linked to the subject.

Study population

The study population was derived from our electronic database of all consecutive patients who underwent ST (Visor-tracheostomy and Bjoerck-flap technique) in a primary ENT unit. Two groups of perioperative intravenous antimicrobial prophylaxis (Clindamycin 600 mg 3 × daily vs. other antibiotics) were compared due to occurred wound infections of the tracheostomy. Other antibiotics were Ceftriaxone 2 g (administered once/day), Piperazillin/Tazobactam 4/0,5 g (administered 3x/day), Cefuroxime 15 g (administered 3 × /day), Levofoxacine 500 mg (administered twice/day), Ampicillin/Sulbactam 3 g (administered 3 × /day), Meropenem 1,5 g (administered 3 × /day), Ciprofloxacin 400 mg (administered twice/day), and Vancomycin 1 g (administered twice/day) (see Table 1). The antimicrobial spectrum varies between those agents, therefore we summarized it for the most commonly used antibiotics in Table 2. The STs mostly conducted within HNOS between 2012 and 2020, were analysed. Experienced surgeons with training level “expert” (> 15 years HNS) performed the STs within HNOS. Within 2012 and 2020 we analysed the quantity of ST-SSI in association with the POAP with Clindamycin. The ST-SSI were primarily diagnosed by ward doctors attended by consultants on their daily ward round. A ST-SSI was defined by peristomal redness and swelling with or without purulent secretion. Those criteria were applied to identify SSIs within our charts. Further, our “Tracheostomy care”-SOP (standard operating procedure) implicates the insertion of a PVC-based cuffed tube and dictates the first decannulation and tube change after 48–72 h after tracheostomy. This was constant over the observation period.

Table 1 Postoperative usage of antibiotics in ST

| Antibiotic                        | N (%)   |
|----------------------------------|---------|
| No antibiotic treatment          | 69 (15,65%) |
| Ceftriaxone                      | 44 (9,98%)  |
| Clindamycin                      | 67 (15,19%) |
| Piperazillin/Tazobactam          | 226 (51,25%) |
| Cefuroxime                       | 7 (1,59%)   |
| Levofoxacine                     | 1 (0,23%)    |
| Ampicillin/Sulbactam             | 17 (3,85%)   |
| Meropenem                        | 8 (1,81%)    |
| Ciprofloxacin                    | 1 (0,23%)    |
| Vancomycin                       | 1 (0,23%)    |
| **Total**                        | **441 (100%)** |
Data collection and statistical analysis

We retrospectively evaluated patient charts and operation protocols. Relevant data were collected: gender, age, surgical tracheostomy technique, postoperative antibiotic treatment and occurrence of tracheostomy site wound infections.

We counted and classified the postoperative wound infections within the first inpatient stay after the tracheostomy.

In all patients where a wound infection occurred, antibiotics where used. We clustered the occurred wound infections in two groups Clindamycin use [yes; no] and other antibiotics used [yes; no] and evaluated the counts (see Fig. 1). The focus of our analysis lied on the question of whether Clindamycin or other antibiotics, did result in a higher quantity of ST-SSIs. We compared the risks of observing a SSI, first, without any adjustment for other potential risk factors, and in a second step, adjusting for age, gender, tracheostomy technique (Visor-tracheostomy vs. Bjoerk-flap technique) and Clindamycin use. In this second step, we chose a logistic regression model. In all steps, we estimated the Odds Ratio with the corresponding two sided 95%-confidence interval.

Reported \( p \) values were obtained by Fisher’s Exact Test for Count Data and, in case of logistic regression models, by the usual Wald-tests (\( z \) approximation). The level of significance is set to 5%.

We performed a purely descriptive data analysis using the software R version 4.1.1 (2021–01-30).

Results

Our data set comprised a total of 453 tracheostomies, 161 were carried out using the Bjoerk-flap technique (BTS) and 292 were Visor-tracheostomies (VT). The majority (72.41%) of our patients was male. The mean age of the patients was 63 years (sd = 12.7 years). All our patients who established a ST-SSI received antibiotic treatment. The SSIs in ST occurred between the fourth on the eighth postoperative day. (MWVT = 7 vs. MWBTS = 6; 95% CI: [− 2, 3]).

Risk of establishing a SSI

Due to a lack of recording we excluded 12 patients from our analysis. Of a total of 441 patients receiving a ST, wound infections occurred in 43% of all the cases, whereof a total of 14% of the patients received Clindamycin and 29% other antibiotics. (\( p = 0001 \)) 156% overall patients did not receive POAP. After exclusion of the patients who did not receive POAP, 1813% overall received Clindamycin (see Fig. 1).

Risk of establishing a SSI with clindamycin

In question if Clindamycin cause more SSI - when looking at the ST collective receiving antibiotic treatment- we saw a statistically significant (Fisher’s \( p = 0008 \)) two time-elevation (9% vs. 43%) of SSI in patients receiving Clindamycin compared with patients receiving other antibiotics (see Fig. 2). Our data analysis seems to support the hypothesis of Clindamycin being a risk factor for wound infection.
Even though the effect is statistically significant, at this point we cannot conclude that Clindamycin is responsible for a higher SSI risk without considering other factors like gender, ST-technique and age. To this end we used a logistic regression model where the dependent variable wound infection is adjusted to gender, age and ST-technique. We found no statistically significant (Fisher’s \( p = 0.004 \)) influence of Clindamycin on ST-SSI with an OR = 2.91 with two-sided 95% confidence interval [0.98; 7.79] (see Fig. 3).

Figure 2: Does Clindamycin cause more wound infections in ST?

Figure 3: The influence of Clindamycin on wound infection in ST in patients receiving antibiotic treatment

Discussion

Surgical tracheostomy (ST) within major head and neck oncologic operations (HNOS) remains the favorable technique to protect the airway and prevent from postoperative asphyxia [14]. As shown before, we used two techniques of ST, the Visor-tracheostomy (VT) and the Bjoerk-flap technique (BTS) (\( N_{VT} = 238 \) vs. \( N_{BTS} = 137 \)). Surgical site infection (SSI) is seen as the most postoperative complication [2] and accounts for more than 20% of all healthcare-associated infections [4]. Further, the literature describes a SSI rate after clean-contaminated HNS ranging between 25 and 64% and of polymicrobial origin [6, 24]. In ST, this minor local infection may spread and can cause serious complications like tracheitis, mediastinitis, clavicular osteonecrosis and necrotizing fasciitis [17]. In our data, we showed a total of 43% SSI within our 441 ST patients. Hence this low rate of SSI in ST, POAP in general, seems to reduce the SSI-rate in ST performed within HNOS [9].

Given our data, SSI in ST mostly occurred within 7 days. As recommended by Bartella et al. the POAP for patients undergoing HNOS should be extended, because of a significantly decreased level of SSI in POAP until the fifth postoperative day [24]. All our patients received perioperative antibiotic treatment at least until the seventh postoperative day.

Given the antimicrobial spectrum of gram-positive, gram-negative and anaerobic organisms [12], POAP in HNOS with a first generation Cephalosporine or Amoxicillin-Clavulanate and Ampicillin-Sulbactam are equally effective [11]. In our cases, we used Ceftriaxon (998%) as a third generation and Cefuroxime (158%) as a second generation Cephalosporine. Amoxicillin-Clavulanate was not administered within our study group. Ampicillin-Sulbactam (Unacid©) was used in 385% of the ST cases. Ampicillin-Sulbactam seems to be effective [11] to cover anaerobic microbes and further Piperacillin-Tazobactam, which we used in 51.25% has been described with a positive effect on treating SSI in HNOS [13].

In our ST cases, a POAP with Clindamycin was administered in 15.19%. Our data analysis supports the hypothesis of Clindamycin being a risk factor for SSI.

We could observe a statistically significant (Fisher’s \( p = 0.008 \)) two time-elevated rate (9 vs. 43%) of SSI in patients receiving Clindamycin compared with patients receiving other antibiotics. However, we found no statistically significant influence of Clindamycin on ST-SSI. Even though we were not able to proof a statistically significant association, studies show that Clindamycin is less effective in avoiding SSI compared with Ampicillin-Sulbactam (Unacid©) in HNS [6]. Some studies showed an even higher risk to establish SSI when Clindamycin is used as POAP in HNS [25, 26]. Even a self-reported β-lactam allergy is
associated with an increased SSI risk mediated through receipt of alternate antibiotic prophylaxis [27]. For patients with a true penicillin allergy undergoing HNOS, studies recommend alternative antibiotics, such as cefuroxime, with a broad gram negative coverage [26]. We recommend to evaluate the SSI risk in ST patients receiving Clindamycin as POAP with a prospective study design to support our hypothesis. Further, a recommendation due to alternatives for Clindamycin in Penicillin-allergic patients should be given.

Our study had a few limitations. The retrospective study design -for one- underlays a prospective two-armed controlled clinical trial. Further, STs were performed by more than one surgeon (N = 6); therefore, minimal diverging techniques could have impacted the quantity of SSIs. In retrospective design there was no option to exactly identify the reason for Clindamycin use, for example an evident Penicillin-allergy. There could have been other reasons not to use other antibiotics, which could have impacted the statistical outcome. Due to design, we were not able to exclude previous radiation therapy, obese patients with short necks or patients with chronic uncontrolled diabetes. Hence, we cannot entirely rule out possible undetected sources of bias in our estimations and comparisons.

Acknowledgements On account of Peter Kress MD this publication has been enabled by providing significant information on Head and neck surgery and SSIs. As the head of the ORL-department in Trier, his knowledge, ideas and impact on our study are more than relevant.

Funding Open Access funding enabled and organized by Projekt DEAL. None.

Declarations
Conflict of interest The authors declared no potential conflicts of interest concerning the research, authorship, and publication of this article.

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