ANTIBIOTIC SUSCEPTIBILITY PATTERNS IN POST-OPERATIVE INFECTIONS IN ORAL CANCER PATIENTS IN A TERTIARY CARE CENTRE IN SOUTH INDIA

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ABSTRACT

BACKGROUND
The use of antibiotic prophylaxis in head and neck oncologic surgery has greatly reduced the risk of post-operative wound infection and the corresponding increase in morbidity and health care costs. Aim: To study the culture sensitivity pattern in patients with infections following surgical resection for oral squamous cell carcinoma and the post-operative antibiotic use in a surgical unit at a tertiary centre in South India.

MATERIALS AND METHODS
Retrospective review of case records of all patients who underwent surgical excision for oral squamous cell carcinoma under the Department of General Surgery Unit I, Christian Medical College, Vellore from January 1, 2013 to December 31, 2013. Statistical Analysis-Epidata® was used for data entry and SPSS 20® was used for data analysis.

RESULTS
A total of 86 patients underwent surgical excision of oral squamous cell carcinoma in 2013, which included 57 males and 29 females. Majority of these patients were within 41 years to 60 years of age (Range: 25 - 82 years). Thirty-five patients had carcinoma of the tongue followed by 29 with carcinoma of buccal mucosa, 17 patients with carcinoma of alveolus, 2 patients with carcinoma of lower lip, 2 patients with carcinoma of retromolar trigone and one patient with carcinoma of the floor of mouth. Thirty-three of these underwent primary closure following resection, 28 of them needed a regional flap, 14 of them underwent microvascular free-flap reconstruction and 11 needed local flaps for closure of the defect. Pseudomonas aeruginosa was the most common organism found in surgical site infections in these patients at our centre followed by other non-fermenting gram-negative bacteria and Staphylococcus aureus. Most pus cultures were polymicrobial. Pseudomonas aeruginosa was also the most common organism causing urinary tract infections in post-operative patients followed by Enterococcus and Klebsiella.

CONCLUSION
There was no statistical association between the infection rate and the site of operation or the type of operation. The surgical site infection rate was 12.8% with Cefoperazone-Sulbactam and Metronidazole antibiotic prophylaxis. The infection rate was higher when regional and microvascular free flaps were used for reconstruction of the primary defect. Since the cultures are polymicrobial with predominant gram-negative organisms, Cefoperazone-Sulbactam is a better antibiotic cover than Cefazolin.

KEY WORDS
Oral Cancer, Surgical Site Infection, Post-Operative Infection, Peri-Operative Antibiotic.


BACKGROUND
Infection found in the surgical site following operation of that part of the body is referred to as surgical site infection. These can sometimes be superficial infections involving the skin only or more serious infections involving tissues under the skin, organs or implanted material. Post-operative surgical site infections prolong hospital stay, increases cost of treatment, delays adjuvant therapy in patients with malignancies and significantly affect the morbidity of patients.
infection rate with this array of organisms inhabiting the operative bed. Not surprisingly, post-operative wound infection rates ranging from 59 to 75% following major head and neck surgery have been reported. A double-blinded, randomised controlled study by Johnson JT showed a significant wound infection of 1.5% of all patients who underwent major onologic head and neck surgery. (9) Therefore, the risk of post-operative surgical site infection has decreased with the use of antibiotic prophylaxis in head and neck onologic surgery. This also prevents the increase in morbidity and treatment costs. Antibiotic prophylaxis has reduced the risk of severe wound infections by approximately 50%. (9) Conversely, inappropriate perioperative use of antibiotics increases costs and risk of antibiotic resistance.

Several small randomised, controlled trials significantly lower infection rates in the prophylaxis groups (5.8 - 38%) compared with high infection rates in placebo groups (24 - 78%) using a variety of regimens including cefazolin, third-generation cephalosporins and ampicillin plus Cloxacillin. Although, these were small studies, the results were concordant and the high rate of infection made the studies to attain statistical significance despite the small sample sizes. Similar results were seen in several other small, uncontrolled studies. (10-12) Antimicrobial prophylaxis targets the bacterial flora that commonly inhabit upper aerodigestive tract and the skin. It was found to be useful only in clean contaminated head and neck surgery. Broad spectrum antibiotics give the best coverage. (13)

Several randomised, single-centre studies have compared antimicrobial regimens for clean-contaminated procedures. In a study, 189 patients who were planned for head and neck cancer procedures were randomised to receive amoxicillin-clavulanate (n = 97) or cefazolin 1 g (n = 92). In both the groups, antibiotics were given within one hour of incision and every eight hours post-operatively for three doses. This study showed an overall wound infection rate of 22%. The risk of post-operative infection was more influenced by the type of surgical procedure than by disease stage. There were no significant differences between amoxicillin-clavulanate or cefazolin used as perioperative antibiotics.

Two studies have compared ampicillin-sulbactam to clindamycin and yielded discordant results. One study of 242 patients (169 evaluable) undergoing head and neck cancer procedures compared ampicillin-sulbactam 1.5 g (n = 119) and clindamycin 600 mg (n = 123) given within one to two hours of incision and every six hours post-operatively for a total of four doses. (14) No difference in surgical site infection rate was found, with 15 infections reported in each group (13% for the ampicillin-sulbactam group and 12% for the clindamycin group). There was no significant difference in adverse events between groups.

Fennessy BG et al compared ampicillin-sulbactam with clindamycin. This study with 212 patients who were planned to undergo clean-contaminated head and neck cancer surgery found lower infection rate in the ampicillin-sulbactam group (13.3%) in comparison to the clindamycin group (27.1%, p = 0.02). (15) A greater number of gram-negative organisms were recovered from patients randomised to the clindamycin group. The combination of gentamicin and clindamycin was found to be superior to cefazolin in one of the older clinical trials. (10) The most frequently isolated pathogen in the wound infections was beta-lactamase producing Staphylococcus aureus. (9) In a study by Becker GD et al, the most common pathogenic aerobes isolated from infected wounds were Staphylococcus aureus and beta-Streptococcus not group A, as well as a variety of Gram-negative organisms. The most common anaerobic isolate was Bacteroides melaninogenicus. (15) Gram-negative bacteria were more often isolated with Pseudomonas aeruginosa as the dominant species.

MATERIALS AND METHODS

Type of Study
Retrospective online chart audit. This study was reviewed and approved by the Institutional Review Board of the Christian Medical College, Vellore.

Inclusion Criteria
All patients who underwent surgical resection for oral squamous cell carcinoma under the Department of General Surgery Unit I from January 1, 2013 to December 31, 2013.

Method of Collection of Data
Retrospective online chart review.

Statistical Software and Analysis
EpiData was used for data entry and SPSS 20 was used for data analysis.

RESULTS
A total of 86 patients who underwent surgical excision of oral squamous cell carcinoma at our institute in 2013 that included 57 males and 29 females. Majority of the patients were within 41 years to 60 years of age (Range: 25 - 82 years), Figure 1. Thirty-five patients (41.9%) had carcinoma of the tongue followed by 29 (32.6%) with carcinoma of buccal mucosa, 17 patients (19.8%) with carcinoma of alveolus, 2 patients with carcinoma lower lip, 2 patients with carcinoma of retromolar trigone and one patient with carcinoma of floor of mouth. Thirty-three of these underwent primary closure following resection, 28 of them needed a regional flap, 14 of them underwent microvascular free flap reconstruction and 11 needed local flaps for closure of the defect.

Free flap and regional flap surgeries were most commonly associated with a wound infection rate of 21.4%, Figure 2. Buccal mucosa resection surgeries and alveolar resection surgeries were most commonly associated with wound infections at 17.2% and 35.3%, respectively. Infection rate in resection surgeries among other sites including tongue, lip, retromolar trigone and floor of mouth was nil.

Antibiotic Administration Pattern
The most common peri-operative prophylactic antibiotic Cefoperazone-Sulbactam and Metronidazole was received by 83 patients. 2 patients received amoxicillin-clavulanic acid and metronidazole as perioperative antibiotic, while one patient received Gentamicin and Metronidazole as perioperative antibiotic.

During the post-operative period, four patients received Piperacillin-Tazobactam and two patients received Meropenem therapeutically for infections based on cultures and antibiotic sensitivity patterns.

Surgical Site Pus Culture
The most common organism isolated from pus cultures was pseudomonas aeruginosa followed by non-fermenting gram-negative bacteria other than Pseudomonas and Staphylococcus aureus, Table 1. Pseudomonas aeruginosa was found susceptible to Cefoperazone-Sulbactam and Piperacillin-Tazobactam. Only patients in whom surgical site infection was suspected clinically were subjected to pus culture from surgical site, Table 2.

Urine Culture
The most common organism causing urine infection in our study was Pseudomonas aeruginosa, Enterococcus and E. coli. Pseudomonas aeruginosa was susceptible to Cefoperazone-Sulbactam and Enterococcus was susceptible to Linezolid, Tables 3 and 4.

Sputum Culture
There were totally 4 sputum cultures sent and one of it showed no growth. Two showed polymicrobial and the fourth sputum culture was monomicrobial. The organisms found in sputum culture were Pseudomonas aeruginosa, Enterococcus, Acinetobacter baumannii, E. coli and Klebsiella.

Blood Culture
There was no growth in any of the blood cultures sent as a part of post-operative infection workup.

A total of 16 pus cultures were sent for 13 patients with suspected surgical site infection. Eleven cultures were positive, of which 9 showed polymicrobial growth. All the patients who had growth in the pus culture had Cefoperazone-Sulbactam and Metronidazole as an intra-op antibiotic. Out of the 11 positive pus culture patients, 5 were operated for carcinoma of the buccal mucosa and 6 were operated for carcinoma of the lower alveolar. Of the 11 patients with positive pus cultures 6 had regional flap reconstructions, 3 had microvascular free flap reconstructions and 2 had primary closure of their defects.

Chi-square between infection and subsite (p-value: 0.155) showed no significant association. Similarly, Chi-square between infection and type of operation (p-value: 0.478) did not show any significant association.

Organism | Number of Cultures
--- | ---
Pseudomonas aeruginosa | 6
Non-fermenting GNB | 5
Staphylococcus aureus | 5
Enterococcus | 3
Yeast | 3
Klebsiella | 2
Enterobacter | 1
E. coli | 1
Candida glabrata | 1
Coagulase-negative Staphylococcus | 1
No growth | 2

Table 1. List of Organisms Grown in Post-Operative Pus Cultures

Note: The no. of cultures is not equal to no. of organisms as each culture can grow more than one organism.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Pseudomonas aeruginosa (n=6)</th>
<th>Non-Fermenting GNB (n=5)</th>
<th>Staphylococcus aureus (n=5)</th>
<th>Enterococcus (n=3)</th>
<th>Klebsiella (n=2)</th>
</tr>
</thead>
</table>
Piperacillin | 83% | 0% | 0% | 0% | 0% |
Amikacin | 50% | 0% | 0% | 0% | 0% |
Ceftazidime | 83% | 0% | 0% | 0% | 0% |
Cefoperazone  |  66% |  40% |  50% |  100%  
Levofloxacin  |  50% |  0%  |  50% |  100%  
Tobramycin    |  50% |  60% |  100%|  100%  
Colistin      |  100% (n=1) |  100% (n=3) |  
Imipenem      |  100% (n=1) |  
Netilmicin    |  66% (n=3) |  100% (n=3) |  
Oxacillin     |  50% |  0%  |  100%|  100%  
Tobramycin    |  50% |  60% |  100%|  100%  
Colistin      |  100% (n=1) |  
Imipenem      |  100% (n=1) |  
Netilmicin    |  66% (n=3) |  100% (n=3) |  
Oxacillin     |  50% |  0%  |  100%|  100%  
Tobramycin    |  50% |  60% |  100%|  100%  
Colistin      |  100% (n=1) |  
Imipenem      |  100% (n=1) |  
Netilmicin    |  66% (n=3) |  100% (n=3) |  
Oxacillin     |  50% |  0%  |  100%|  100%  
Tobramycin    |  50% |  60% |  100%|  100%  
Colistin      |  100% (n=1) |  
Imipenem      |  100% (n=1) |  
Netilmicin    |  66% (n=3) |  100% (n=3) |  
Oxacillin     |  50% |  0%  |  100%|  100%  
Tobramycin    |  50% |  60% |  100%|  100%  
Colistin      |  100% (n=1) |  
Imipenem      |  100% (n=1) |  
Table 2. Sensitivity Pattern for Pus Culture Organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of Cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>2</td>
</tr>
<tr>
<td>E. coli</td>
<td>2</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>1</td>
</tr>
<tr>
<td>Candida tropicalis</td>
<td>1</td>
</tr>
<tr>
<td>No growth</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 3. List of Organisms Grown in Post-Operative Urine Cultures*

*Total number of urine cultures sent = 13.
Note: The number of cultures is not equal to the number of organisms, as each culture can grow more than one organism.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Pseudomonas sp. (n=2)</th>
<th>Enterococcus (n=2)</th>
<th>E. coli (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Cefoperazone</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>100% (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netilmicin</td>
<td>100% (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin</td>
<td>100% (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>100% (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>100% (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>100%</td>
<td>50%</td>
<td>100%</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>100%</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>100%</td>
<td></td>
<td>100%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Sensitivity Pattern for Urine Culture Organisms

DISCUSSION
In 2013, 86 patients underwent surgical resection for oral squamous cell carcinoma. All of these patients were included in the study. The most common prophylactic antibiotic given was Cefoperazone-Sulbactam and Metronidazole, started at induction and continued for 48 hours post-operatively. In the post-operative period, patients having symptoms and signs suggestive of infection underwent a complete evaluation and workup to identify the source. The surgical site infection rate was found to be 12.8%.

The most common organisms isolated in pus cultures were Pseudomonas aeruginosa (35.2%), other non-fermenting Gram-negative bacteria (29.4%) and Staphylococcus aureus (29.4%). Of the 16 patients for whom pus cultures were sent, only 3 patients had a urine culture also sent as a part of fever workup. In those three patients, only one patient grew E. coli along with yeast and other two urine cultures were sterile. Of these 16 patients, only four patients had a blood culture also sent as a part of a fever workup. None of the blood cultures had growth of any significant organisms.

A total of 13 patients were suspected to have a urinary tract infection, urine cultures were sent, and the most common organism was Pseudomonas aeruginosa, Enterococcus and E. coli. Of the subsites, 17.2% of patients operated for buccal disease developed cultures with the growth of significant organisms in pus and 35.3% of patients operated for carcinoma of the alveolus developed cultures with the growth of significant organisms.

Complex reconstructive techniques using regional flaps and microvascular free flaps were associated with wound infections with pus cultures growing significant organisms in 21.4% of patients. Only 6% of patients undergoing primary closure had significant growth in pus cultures.
The Limitations of this Study were as follows:
- This study was a retrospective and was conducted for a period of 1 year and so the sample size is small.
- Due to subjective differences in preparing the operation notes and discharge summaries, certain data was inadequate to be taken into audit like duration of surgery and details regarding catheterisation.

CONCLUSION
Cefoperazone-Sulbactam with Metronidazole is an effective antibiotic prophylaxis for head and neck cancer patients. The surgical site infection rate was 12.8% with Cefoperazone-Sulbactam and Metronidazole antibiotic prophylaxis. Antibiotic prophylaxis should be given at induction during surgery and continued post-operatively for at least 48 hours. Since the most common organism in our clinical practice at our institution is Pseudomonas aeruginosa sensitive to Cefoperazone-Sulbactam, it is an effective perioperative antibiotic cover.

Recommendation
Since the cultures are polymicrobial with predominant gram-negative organisms, Cefoperazone-Sulbactam is a better antibiotic cover than Cefazolin. The infection rate is higher in the free flap and regional flap surgeries suggesting povidone-iodine scrub preparation of parts might help in decreasing infection rates.

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REFERENCES