

Postoperative infectious complications in head and neck cancer surgery



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AIM: *In our work we have considered the problems related to the post-operative hospitalization in patients admitted to our ENT's department in the last 4 years.*

MATERIAL OF STUDY: *Our observations refer to a sample of 155 patients suffering from head and neck tumors.*

RESULTS: *Regarding therapy, some drugs have been less effective to prevent post-operative infection: the ceftriaxone at the level of the oral cavity/oropharynx and ceftriaxone/pefloxacin at the level of the hypopharynx/larynx.*

DISCUSSION: *Post-operative infections in cancer surgery can compromise not only the surgical outcome but also be responsible for delays for any adjuvant treatments. Post-operative infections risk in head-neck cancer surgery drops from 30-80 % to 20 % with perioperative antibiotic prophylaxis. Despite the introduction of pre-operative prophylaxis, according to guidelines, the number of post-surgical infections still remains high (40/61% of cases). It is important to know the intrinsic risk factors (related to the patient) and extrinsic (related to the external environment and the same procedure) to better understand how to prevent infections. Prolonged hospitalization can expose patients to the risk of hospital pathogens.*

CONCLUSION: *We tried to outline a profile of head-neck cancer patients more likely to contract post-operative infections. We also compared the effects of various antibiotics administered before and after the onset of complications to suggest a therapeutic protocol.*

KEY WORDS: Antibiotics therapy Post-operative infectious, Prophylaxis in head and neck surgery

Introduction

The risk of post-operative infection in head and neck oncological surgery is related to the peri-operative exposure of the wound to bacteria¹. The organisms involved are usually the patient's own commensal bacteria colonizing mucous membranes and skin.

It can result in wound breakdown and the formation of mucocutaneous fistulae leading to increased morbidity,

prolonged hospitalization and even death with an increase in health care costs. Significant surgical site infection can delay the administration of adjuvant therapies (chemotherapy and radiotherapy), which increases the risk of tumor recurrence¹. In the literature, numerous Authors who have dealt with this issue have sought to identify risk factors that promote infectious complications. In particular, they have found that there are about 30-80% cases of infection in operated patients for the head and neck cancer, without peri-operative prophylaxis. This percentage insignificantly decreases to 20% with correct antibiotic prophylaxis¹.

Another important factor considered in the literature for the successful execution of ENT cancer surgery is the prevention of post-operative infection at the surgical site by the surgeon and surgical team.

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So prophylactic antibiotics are given at the time of surgery to reduce the incidence of post-operative surgical site infections. The aim is to have therapeutic levels of antibiotic in the tissues at the time of surgical incision. This prevents any organisms that inevitably contaminate the wound during the surgical procedure establishing infection.

However, the use of antibiotics in this way (to prevent rather than cure infection) is associated with increased costs, risks of adverse reactions and may lead to the development of antibiotic resistant organisms or *Clostridium difficile* colitis. The emergence of resistance is a major public health problem, and the unnecessary or excessive use of antibiotics must be eliminated.

There is a good evidence for antibiotic prophylaxis in clean/contaminated head and neck oncological surgery. Current guidelines recommend that prophylaxis should be started pre-operatively, ideally within 30 min of the induction of the anesthesia. They recommend the duration of prophylactic antibiotics should not be more than 24h and should provide broad spectrum antimicrobial cover for aerobic and anaerobic organisms.

Despite this infection rates are still reported in up to 40-61% of cases.

In general, interventions can be classified into four classes according to the level of bacterial contamination and subsequent incidence of post-operative infections. More precisely they can be divided into:

- *clean procedures*: when the respiratory, intestinal or genito-urinary mucosa's continuity is not violated and there is an absolute respect for asepsis, in the operating room;
- *clean/contaminated procedures*: when the continuity of the respiratory, intestinal or genitourinary mucosa is violated, but without losses of organic materials to outside;
- *contaminated procedures*: in which there are signs of acute inflammation (without pus), or where there is a visible wound contamination, such as copious losses of material by internal organ during surgery or composed/open wounds (occurring less than 4 hours before surgery);
- *dirty procedures*: carried out in presence of pus or perforated internal organ or composed/open wounds (occurring more than 4 hours before surgery).

Clean-contaminated procedures, where bacterially colonized mucosal surfaces are breached, such as occurs during head and neck oncological surgery, have a higher incidence of post-operative infections than 'clean' procedures, where such breaches do not occur.

The incidence of wound infections after clean-contaminated surgery, without the administration of pre-operative antibiotics, ranges from 30 to 80% depending on the patient cohorts and procedures analyzed¹. The use of appropriate prophylactic antibiotics in head and neck oncological surgery has been reported to reduce infection rates from 85 to less than 10%¹.

The problem of post-operative infection is not significant during clean procedures, in which even without

peri-operative antibiotic therapy the sepsis percentage is considered just 1%².

In the literature, five classes of surgical site infections were defined³, ranging from a regular post-operative condition (class 0) to the pharyngo-cutaneous fistula (PCF) (class 5).

In particular⁴:

- 0: no erythema or induration of the surgical wound;
- 1: presence of erythema around the suture line limited to 1 cm;
- 2: presence of erythema and induration between 1 and 5 cm;
- 3: presence of erythema greater than 5 cm and induration;
- 4: purulent drainage, even spontaneously, by wound or self-priming drainage or during aspiration of secretions by drainage;
- 5: pharyngo-cutaneous fistula (PCF) or muco-cutaneous fistula.

In post-surgical infections of the oral cavity and oropharynx, the agents most commonly relevant are^{5,6}:

- *Gram + bacteria*: including *Streptococcus Viridans*, *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, *Staphylococcus Aureus*, *Peptostreptococci* (anaerobic), *Bacteroides oralis* (anaerobic), *Veillonella* (anaerobic), *Actinomyces* (anaerobic);
- *Gram - bacteria*: including *Escherichia coli*, *Bacteroides* (anaerobic), *Fusobacterium* (anaerobic), *Pseudomonas aeruginosa*, *Enterobacteriaceae*, *Haemophilus*;
- *Fungi*: including *Candida albicans*.

In wound infections after laryngeal surgery, the agents most involved² are:

- *Gram + bacteria*: *Staphylococcus aureus* and *epidermidis*, *Streptococcus Species*, *Corynebacterium species*, the *Peptostreptococcus species*;
- *Gram - bacteria*: *Haemophilus influenzae*, *Neisseria species*, *Moraxella species*, *Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides* (anaerobic), *Fusobacterium* (anaerobic).

The knowledge and consideration of other risk factors reported in the literature is important for prevention of post-operative infections.

In particular, the hospitals risk factors can be divided into:

- Intrinsic, related to the patient: age (increased age), Sex (male gender), the luxuries habits (tobacco and alcohol history), the underlying disease to other organs, the oncological disease (tumor site, size and stage), the nutritional status (poor one with low body mass index);
- Extrinsic, related to the environment or various procedures (pre-, intra-and post-operative): length of post-operative hospital stays, type of intervention (intraoperative flap reconstructions, tracheoesophageal puncture and pre-operative tracheostomy), presence of the drainage at the operative site or urethral catheters.

The first risk factor considered is the **elderly age**. It promotes septic complications: in fact, in patients older than 60 years, the risk of infection is 6 times higher than younger subjects ⁷.

The reasons are a lower immune system function at the loco-regional level (decrease of non-specific local defenses) and less lymphocytic activity. In addition, the presence of concomitant systemic disease and lower metabolic capacities, especially in patients with more advanced age, are undoubtedly favoring conditions for infectious complications.

As regards **sex**, males have a probability 4 times greater than the female to be hit by infections in the postoperative period ⁸. This relationship is particularly evident in the case of oral cavity, oropharynx cancer (in old age), larynx and salivary glands both in the case of mortality and morbidity.

The luxuries habits, such as alcohol abuse and smoking, are carcinogenic factors and patients with high risk of surgical infection often have an history of consumption of these substances and of alcohol liver disease ⁹.

Among the underlying diseases, the one most related to the risk of infection after surgery is **diabetes**: in fact, people with diabetes have a risk of infection of 50% higher compared to normoglycemic. This is due to difficulty of reparative processes and to deficiency of the immune system (such as abnormalities of phagocytosis, chemotaxis, bactericidal power of neutrophils, proliferation and neof ormation of capillaries, etc.). According to some Authors it is caused by hyperglycemia that would favor the non-enzymatic glycosylation with enzymatic alteration of proteins and, therefore, there would be a delay in healing and susceptibility to infections; the hyperglycemic blood serum would facilitate the growth especially of Gram + ¹⁰. Diabetes, according to other Authors, is closely associated with pharyngocutaneous fistulas and stroke ¹¹. Of equal importance to diabetes in the onset of infection is **anemia**, both pre-operative and post-operative for the higher incidence of surgical site infection ¹². In this case, the infection would be favored by low oxygen tension tissue. In a large series, including also non-ENT interventions (756 ENT interventions on a total of 6301), another Author, Dunne, noted that preoperative anemia was related to an increase of postoperative surgical wound infection, to an onset of pneumonia and the prolongation of hospital stay ¹².

Regarding the **oncological pathology**, the presence of a large tumor involves a greater risk of post-operative infections. This is due to malnutrition, which is often associated with pain and dysphagia that are typical of advanced cancer, to the immune system impairment, to an extensive demolition of the tissues with the greatest difficulties in the reconstruction time ¹³.

In addition, malnutrition, compromising the immune system and protein synthesis, retards the healing process. A decrease of more than 20% of the ideal weight involves a double risk of post-operative infection ¹⁴. In a case

series, reported by Robbins, comprising 400 patients operated for cervical-facial tumors, 63 patients (19.75%) developed surgical wound infections: among factors related to the patient, in addition to alcohol, is mentioned malnutrition that determined also a lower resistance to surgical insult with increased risk of intra-operative mortality ¹⁵.

It was found that after 48 hours of hospital stay, the patient's skin is colonized by bacteria of nosocomial origin (Scottish Intercollegiate Guidelines Network (SIGN) of 2008) ⁷.

They are often antibiotic-resistant germs, which can promote contamination during surgery, with consequent prolongation of hospital stay.

Sources that facilitate the contact with germs such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella*, *Staphylococcus*, *Bacillus* Species, are sinks, sanitary and sills.

It was assumed that the change in diet and physical activity during hospitalization would result in a change in the bacterial flora of the upper airways, upper digestive and around intestines, promoting infections (endogenous germs) ¹⁰.

It was found that prolonged hospitalization facilitates the onset of complications, such as:

– the faringocutaneous fistula, post-operative bleeding for direct erosion of carotids ¹¹. Regarding type of intervention, the need of complex procedures for the presence of a large neoplasm in relation to T which involves the preparation of a flap, increases the likelihood of surgical infection ³. Despite prophylactic treatment with antibiotics, however, it has been reported, an infection rate of 20-25% in the contaminated cervico-facial interventions that require flaps while in same interventions without the use of flaps these percentage drops to 5-10% ¹⁶.

Moreover, in the case of radical surgery, the surgical site can be cleaned from saliva, resulting in failure of the wound in the postoperative period: this condition necessarily predisposes to infectious complications ⁴.

The dehiscences more frequent in the case of oncological surgery of the oral cavity, are caused by movements of the tongue, ischemia of the suture line, by direct closure with excessive traction of mucous residues margins, by necrosis and ischemia of the reconstructive flaps and, finally, by errors of surgical technique ⁶.

The rate of infection increases in the case of surgical procedures with neck dissection especially, in the case of bilateral neck dissections: it can be attributed to the increased interruption of blood circulation in the case of bilateral neck dissections ¹⁷.

The tracheotomy facilitates the onset of tracheobronchial infections both the reduction of the mechanical and immunological defenses of the upper airways and for the aspiration of secretions (40.8% in patients with tracheostomy compared to 23.8% of patients without tracheotomy) ⁷.

The type of intervention is related to the duration of the same: the probability of infection doubles every hour in the case of clean-contaminated operations; this is due to an increased exposure to environmental contamination, to the greater tissue damage and to incorporation of germs into the wound by the glycoprotein film that forms on tissues and whose increase is directly proportional to the time of exposure to air ⁷.

Also, the use of drainage or other materials (es. sutures) or surgical devices increases the rate of infection.

For example, the nasogastric tube facilitates the inhalation of secretions and esophageal sphincter incontinence with possible development of gastroesophageal reflux ¹.

In addition, it is preferable that the drainages positioning is different from the surgical incision. The prolonged maintenance of drainage increases the risk of surgical site infections, even in the case of cleaned neck dissection ¹. The bacterial colonization of drainages occurs during their preparation, the periodic replacement of post-operative collection containers and the stagnation of drainage material ⁶.

In the post-operative period, it is essential to adopt a number of measures such as the control of drainage, the cleaning of the tracheostomy, a good rehydration and a right nutritional support to prevent complications ¹⁸.

SCOPE OF WORK

The purpose of this work is to consider issues related to the postoperative hospital stay of patients admitted to our Department of Otolaryngology in the last 4 years. We examined various significant factors for their correlation with the eventual emergence of infectious and hemorrhagic complications in the post-operative course of patients undergoing oncological head and neck surgery. Then different factors were correlated to literature data. According to the different parameters analyzed, we will try to outline a profile of head and neck cancer patients with increased risk of complications during post-operative period.

Moreover, the results obtained by different antibiotics or other drugs administered in the period before during and after the onset of infectious complications were compared to suggest an effective therapeutic protocol in countering the microorganisms most involved in these infectious processes.

Materials and Methods

Our observations refer to a sample of 155 patients suffering from head and neck tumors. We have studied patients with oral cavity, oropharynx, salivary gland, larynx and hypopharynx tumors undergoing surgical treatment for tumor excision, in the period between September 2010 and August 2018 at the Department of

Otolaryngology, University of Naples "Federico II".

We have considered cases in which there has been an infectious or hemorrhagic postoperative complication and then it was calculated their incidence.

Different factors were considered for each of these subjects, some relative to the patient and the preoperative status, others related to the postoperative course.

And, in the pre-operative period we have considered:

- sex
- age
- nutritional status
- the underlying disease
- the oncological disease

in the postoperative period:

- laboratory tests
- the type of intervention
- the duration of the intervention
- the presence of catheters or drainages

Regarding to **sex**, 126 (75.5%) were males and 41 (41.5%) females, while the overall age was of 60.3 years, 61 years for males (range 40-81) and 56.3 years for females (range 38-76).

The overall average weight was 70 kg: 70,69 kg for males (range 45-112) and 61.25 kg for women (4 patients).

Among **underlying diseases**, in reference to the patients considered, in all cases it was observed that the heart diseases (hypertension, IMA, angina, atrial fibrillation, etc..) were the most frequent (95; 56.9%), less frequently the lung diseases (68, 40.7%), with prevalence of chronic obstruction pneumonia disease (COPD), diabetes (25; 14.9%), liver diseases (25; 14.9%, 23 cases on viral basis and 2 cases on alcohol basis), kidney disease (14; 8.4%).

About the **oncological pathology**, histological types, at the level of the oral/oropharynx cavity were in the majority squamous cell carcinomas (8/9, 88.9%; 2/9, 22.2% with basaloid aspects) and one case (11.1%) of salivary glands epidermoid carcinoma. At the level of the salivary glands we mainly recorded, in the case of parotid gland, pleomorphic adenomas (60.5%), cistoadenolinfomas (Warthin tumors) (36.8%), one case of squamous cell carcinoma (2.3%). At the hypopharynx/larynx level, 97% of cancers are squamous cell carcinomas (15% with basaloid aspects and 2% with verrucoid aspects), a clear-cell carcinoma, a neuroendocrine carcinoma and a dyskeratosis with images of carcinoma in situ and infiltrating one, at the level of neck dissections we have found 12 (85.7%) cases of metastatic squamous cell carcinoma and 2 cases (16.6%) of large B-cell NHL.

The TNM of various sites were reported in Table I.

Concerning the laboratory data, parameters that mostly are modified in the post-operative period compared to pre-operative one was:

- **glycemia** increased in 1 patient (11%) with oral cavity/oropharynx cancer and 23 patients (22.3%) with laryngeal cancer;
- **serum iron**, hemoglobin and hematocrit decreased in

6 patients (66.6%) of the oral cavity/oropharynx district, 89 patients (86.4%) with laryngeal cancer and in 4 patients (28.5%) underwent selective neck dissection; – **Albumin and total protein** decreased in 7 patients (77.7%) with oral cavity/oropharynx disorders, 73 patients (70.8%) with laryngeal tumors and in 2 patients (14.3%) underwent selective neck dissection. The types of surgery, to which patients were subjected, and the average surgery's duration were reported in Table II. The urethral catheter was maintained for 3 days (range 1-13), while the self-suction latero-cervical drainage were removed after 4 days (range 3-15).

Results

The analysis of considered parameters in 155 patients revealed 41 cases (26,45%) with infectious complications. The ratio of complications according to the locations considered is different, as it is apparent from Table III.

At the level of the oral cavity/oropharynx, 6 patients (5 males and 1 female) had infectious complications in the postoperative period, while at the hypopharynx/larynx level 35 patients (31 males and 4 females) had this type of complication.

The surgical procedures of 41 patients examined are summarized in Table IV.

Patients were subjected to surgical wound swab: the isolated germs are shown in Table V.

The onset median interval of infection was 7 days (range 4-10) for oral cavity/oropharynx intervention and 10 days (range 3-22) for hypopharynx/larynx interventions. The average duration of infectious complications was 6 days (range 1-15) for oral cavity/oropharynx surgical procedures and 16.5 days (range 2-68) at the hypopharynx/larynx.

Table VI summarizes the correlations of patients with infectious complications compared to the underlying diseases and total number of patients analyzed for tumor site.

TABLE I - Distribution of various infectious complications according to the primary tumor

Site	Type of complication	Number	%
Oral cavity / oropharynx	Submental fistula	3	50%
	laterocervical purulent collection	2	33,3%
	Left submandibular dehiscence with purulent discharge	1	16,6%
Total		6/9	66,6%
Hypopharynx / larynx	peristomal fistula	23	65,7%
	Purulent collection laterocervical	7	20%
	Purulent collection supraclavicular	3	8,5%
	Submental dehiscence with purulent discharge	1	2,8%
	Purulent tracheal	1	2,8%
Total		35/103	33,9%
flushes laterocervical	none	0/14	0%
salivary glands	none	0/43	0%

TABLE II - Surgical procedures performed in 41 patients with infectious complications

Site	Surgical procedure on T	Number	%
Oral cavity / oropharynx	Pull-Through	4/7	57%
	K tonsillar excision by mandibulotomica	1/1	100%
	K base excision language by faringotomica	1/1	100%
Hypopharynx / larynx	Total Laringectomies	27/70	38,5%
	sovraglottic laringectomies	5/29	17,2%
	reconstructive Laringectomies sec Labayle	3/4	75%

TABLE III - Microorganisms isolated

Site	Microorganism	Number	%
Oral cavity / oropharynx	Staphylococcus aureus	3/6	(50%)
Hypopharynx / larynx	Pseudomonas aeruginosa	8/35	(22,8%)
	Candida albicans	7/35	(20%)
	Aspergillus fumigatus	3/35	(8,5%)
	Corynebacterium steatum	1/35	(2,8%)

TABLE IV - The proportion of patients with complications compared to the underlying conditions

Site	Patients number	Kidney disease	Diabetes	Liver disease	Pulmonary disease	Heart disease
Oral cavity / oropharynx	Total patients	4	3	0	4	4
	Complication patients	2 (50%)	1 (33%)	0	3 (75%)	2 (50%)
Hypopharynx / larynx	Total patients	7	15	18	49	71
	Complication patients	3 (43%)	7 (46%)	4 (22%)	16 (33%)	23 (32%)

TABLE V - Antibiotics and / or antifungal activity in all patients and in those with infectious complications before surgery

Site	Patients number	Average duration of therapy	Antibiotic (patients number)
Oral cavity / oropharynx	total patients: 9	1 Day	Ceftriaxone (2) Ceftazidima (1)
	patients with infectious complications: 6	1 Day	Ceftriaxone (2) Ceftazidima (1)
Hypopharynx / larynx	total patients: 103	2 Days	Ceftazidima (1) Ceftriaxone (19) Ciprofloxacin (2)
	patients with infectious complications: 35	2 Days	Ceftazidima (1) Ceftriaxone (8) Ciprofloxacin (1)

The following tables (Tables VII, VIII) show the mean duration of therapy, types of antibiotics and/or antifungals for total patients and in those with infectious complications both before and after surgery.

Instead, as regards the hemorrhagic complications, 14 cases of bleeding have been registered (12 males and 2 females) occurred in the post-operative course only in the interventions for laryngeal tumors, as is illustrated in Table IX. The site of bleeding origin is shown in Table X.

Bleeding complications occurred about 14 days after surgery (range 1-81).

Patients who presented both types of complications were 8 males. They were undergoing total laryngectomy. Two of eight patients died for bleeding complications.

Discussion

In the study of 155 patients, the incidence of surgical infections in the head and neck oncological interventions was 26.45%, corresponding to 41 cases, while bleeding complications occurred in 9.03% of cases (14 patients). In relation to various pre-operative and post-operative considered parameters, it should be noted that cancer site has a primary role in promoting infectious complications.

In fact, it should be noted that, 6 of 9 cases (66.6%) affected by oral cavity and oropharynx tumors had showed infectious complications and, in particular, in 50% (3 cases) submental fistula, in 33.3% (2 cases) puru-

lent latero-cervical collections and in 16.6% (1 case) dehiscence of the surgical wound.

Moreover, the methods of the surgical technique in these cases, obviously influenced by the greater complexity (sophistication) and duration of surgery, because there was the above complications in 100% of cases when it was necessary to dissect the maxillary bone in the tonsil or tongue base's tumors, compared to interventions in which it wasn't necessary (Pull-Through), where there was a lower percentage (4/7 patients; 57.7%).

Lower incidence of infections has occurred in patients undergoing resection of laryngeal tumors by total laryngectomy (27/70 patients, 38.5%) or supraglottic laryngectomy (5/29 patients, 17.2%).

However, even for laryngeal tumors when we performed reconstructive laryngectomy according to Labayle there was a high rate of infectious complications (3/4 patients, 75%), due to greater difficulty during rehabilitation after surgery.

Peristomal fistulas have occurred in 65.7% of cases (23/25 patients). Rarely in postoperative period, purulent latero-cervical (7/35 patients; 20%) and supraclavicular (3/35 patients; 8.5%) collections have been drained, while dehiscence of surgical wounds recorded in 2.8% of cases (1/35 patients).

There were not complications in the postoperative course of neck dissections or excision of parotid neoplasms by enucleation interventions (superficial or total parotidectomy) with facial nerve preservation.

The most frequently isolated bacteria by swabs, were

TABLE VI - Antibiotics and / or antifungal activity in all patients and in those with infectious complications following surgery in the oral cavity / oropharynx and hypopharynx / larynx.

Site	Patients number	Average duration of therapy	Antibiotic (patients number)
Oral cavity / oropharynx	total patients: 9	25 days	Ceftazidima (1) Ceftriaxone (9) Ciprofloxacina (1) Gentamicina (3) Imipenem/cilastatina (4) Netilmicina (1) Nistatina (3) Pefloxacina (7) Teicoplanina (2)
	patients with infectious complications: 6	30 days	Ceftazidima (1) Ceftriaxone (6) Ciprofloxacina (1) Gentamicina (3) Imipenem/cilastatina (3) Netilmicina (1) Nistatina (3) Pefloxacina (6) Teicoplanina (2)
Hypopharynx / larynx	total patients: 9	18,5 days	Amikacina (1) Amoxicillina (1) Amoxicillina/acido clavulanico (1) Aztreonam (1) Cefepime (1) Cefotaxima (1) Ceftriaxone (9) Ceftazidima (7) Ciprofloxacina (8) Fluconazolo (2) Gentamicina (24) Imipenem/cilastatina (22) Levofloxacina (1) Lincomicina (1) Metronidazolo (1) Netilmicina (6) Nistatina (4) Pefloxacina (41) Piperacillina (3) Rifaximina (1) Teicoplanina (19)
	patients with infectious complications: 6	25 days	Amoxicillina/acido clavulanico (1) Cefepime (1) Ceftazidima (3) Ceftriaxone (34) Ciprofloxacina (6) Gentamicina (14) Imipenem/cilastatina (15) Levofloxacina (1) Lincomicina (1) Netilmicina (2) Nistatina (2) Pefloxacina (25) Piperacillina (2) Rifaximina (1) Teicoplanina (11)

Staphylococcus aureus (3/6 patients; 50%) for the oral cavity/oropharynx and Pseudomonas aeruginosa (8/35 patients; 22.8%) for the hypopharynx/larynx. These data are confirmed by literature in which for head and neck region after surgery the most common organism isolated from clinical specimens was methicillin-resistant Staphylococcus aureus (MRSA) in 43% of cases, followed by Pseudomonas aeruginosa in 36% of cases and serratia marcescens, Proteus mirabilis and Enterococcus faecalis each occurring in 7% of cases ¹.

In our experience, some cases with laryngeal cancer presented mycosis: Candida albicans (7/35 patients, 20%) and Aspergillus fumigatus (3/35 patients; 8.5%).

These infections, both at the level of the oral cavity/oropharynx and larynx occurred after 7-10 days after surgery. However, they treated with antibiotic therapy, resolved within 6 days (range 1-15) in the first sites and within 16.5 days (range 2-68) for laryngeal sites.

These data, in our opinion, are in relation to the deepest infection site in the postoperative course of laryngeal patients that is less prone to curettage during medications and more difficult to treat by medical therapy involving the neck's soft tissues. A significant finding emerged from the evaluation of risk factors related to the patient. In particular, the presence of underlying diseases are unfavorable conditions, in each case, to the post-operative course. The chronic obstructive pulmonary diseases are the most obvious worsening cause for operated patients at the level of the oral cavity and oropharynx (75%) compared to diabetics (46%) and kidney disease patients (43%) operated at the larynx.

However, in all cases, when there are conditions of underlying diseases to other organs, the post-operative course is more prolonged and often favoring infectious complications.

Conflicting data are found in the literature regarding to the underlying conditions: Arriaga (1990) ¹¹ reported a higher percentage of complications in the post-operative course of 384 patients who underwent total laryngectomy among those suffering from chronic obstructive pulmonary disease (68.8%), hypertension (34.6%), alcohol dependence (34.5%) and angina (15.9%); however, specifically, infectious complications of the surgical wound were more frequent in diabetics (11.2%).

On the contrary, Penel (2001)⁵ believe that diabetes is not a risk factor for surgical wound infections: these Authors have found infectious complications in only 6% (1/17 patients), and 11 % (1/9 patients) of diabetics. Instead Gonzalez Aguilar (2001) ¹⁸, as regards the risk of infection after total laryngectomy, has placed emphasis not to underlying diseases such as diabetes or chronic obstructive pulmonary diseases (especially emphysematous), but to parameters such as the intake of alcohol exceeding 1 liter/day, ESR (Erythrocyte sedimentation rate) \pm / = 10mm, serum albumin <3.5 mg%, previous radiotherapy or surgery at the cervical level.

It is obvious that the post-operative course is also con-

ditioned by histologic type of tumor and, in particular, by the extension of the same, in agreement with literature.

In fact, Robbins (1990) ¹⁵ has shown that in case of cervico-facial tumors, infections occur in 8% of T1 (3/37 patients), in 23.4% of T2 (15/64 patients), in 25.7% of T3 (17/66 patients) and in 15.7% of T4 (3/19 patients).

In a sample of 111 patients, all underwent surgery for cervical-facial tumors (89 at the level of the larynx, 8 at the level of hypopharynx, 36 at the level of oral cavity/hypopharynx), Coskun (2000) ¹⁷ found a infection's rate of 0% in patients with stage I, of 19% in those with stage II, of 18% in those with stage III and 43% with stage IV.

Even the pre-operative clinical conditions, especially nutritional status, are important conditions to consider. In particular, debilitated subjects or undernutrition status after surgery have always favored cases of infections and other complications.

Malone (2002) ¹⁹ reported the "low body weight" among factors associated with infection of the surgical site, with a percentage of 12.3% (20/162 patients).

TABLE VII - Bleeding complications in relation to the type of intervention

Type of intervention	Bleeding cases	Percentage
Total Laryngectomy	12/70	17,1%
Sovraglottic Laryngectomy	2/29	6,9%

TABLE VIII - Site of origin of bleeding

Site of bleeding origin	Number
Thyroid region	7/14 (50%)
Lingual Region	3/14 (21,4%)
Internal jugular Vein	2/14 (14,3%)
Oval fossa venous network	1/14 (7,1%)
Tirolinguofacial trunk	1/14 (7,1%)

TABLE IX - Drugs used before of infectious complications onset and more attached to the same

Site	Antibiotic (patients with complication)
Oral cavity / oropharynx	Ceftriaxone (5)
	Gentamicina (1)
	Imipenem/cilastatina (1)
	Pefloxacina (3)
	Teicoplanina (1)
Hypopharynx / larynx	Ceftriaxone (25)
	Ciprofloxacina (1)
	Gentamicina (4)
	Imipenem/cilastatina (5)
	Netilmicina (1)
	Pefloxacina (7)
	Teicoplanina (4)

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Type of intervention	Bleeding cases	Percentage
Total Laryngectomy	12/70	17,1%
Sovraglottic Laryngectomy	2/29	6,9%

TABLE VIII - Site of origin of bleeding

Site of bleeding origin	Number
Thyroid region	7/14 (50%)
Lingual Region	3/14 (21,4%)
Internal jugular Vein	2/14 (14,3%)
Oval fossa venous network	1/14 (7,1%)
Tirolinguofacial trunk	1/14 (7,1%)

TABLE IX - Drugs used before of infectious complications onset and more attached to the same

Site	Antibiotic (patients with complication)
Oral cavity / oropharynx	Ceftriaxone (5)
	Gentamicina (1)
	Imipenem/cilastatina (1)
	Pefloxacina (3)
	Teicoplanina (1)
Hypopharynx / larynx	Ceftriaxone (25)
	Ciprofloxacina (1)
	Gentamicina (4)
	Imipenem/cilastatina (5)
	Netilmicina (1)
	Pefloxacina (7)
	Teicoplanina (4)

Robbins (1990) ¹⁵ reported similar rates only in the case of moderate malnutrition (14.2%, 5/35 patients), while in the case of the average malnutrition the infection rate was 50% (7/14 patients).

In accordance with literature, we believe that the main etiologic factor of purulent post-operative wound inflammations are *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* strains (MRSA) ²⁰⁻²⁸. In fact, *Staphylococcus aureus* was detected in the peristomal area in 46.9% of patients with laryngectomy, while Methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated in 21.9% of cases ⁹.

According to some Authors, in MRSA isolates, high resistance was found to Cefixime (100%) Doxycycline (100%) Oxacillin (96.5%) Gentamicin, (96.3%), Timethoprim/Sulfametoxazole (95.6%) Chloramphenicol (93%) Tobramicin (81.03%), Ofloxacin (72.4%) and Ciprofloxacin (63.7%). Low resistance was found to Ceftazidime (36%), Amoxicillin/Clavulanate (32.7%), Fosfomicin (31%), Cefroxime (24%), Amikacin (17.2%) and Meropenem (13%). One isolate was found to be Vancomycin resistant (MIC 32 µg/ml). Four isolates had intermediate resistance, with two strains having MIC of

16 µg/ml and two having MIC of 8 µg/ml. These strains were also resistant to all the other tested antibiotics except Linezolid to which all isolates were susceptible ¹⁰.

In relation to treatment ²⁹⁻³⁴, considering the drugs used before the onset of complications, it appeared that some of them are more frequently associated with a lower prevention of the same, as is apparent from reading the following table especially for Ceftriaxone and Pefloxacin (Table XI). Instead, the drugs that more often have effectively kept the eradication of infection and a post-operative course without other infectious complications are shown in Table XII.

Conclusions

The study has allowed to perform a retrospective analysis of infectious or septic complications after head and neck oncological surgery.

The knowledge of all factors that determine or contribute to the occurrence of these complications is necessary for a correct diagnosis so that the postoperative hospital stay is shortened, hospitalization expenses are reduced, and we quickly allow that the patient can be enlisted for some adjuvant therapy without compromising prognosis. In the examined sample of 155 patients affected by head and neck cancer, among the factors more related to the development of surgical wound infections, we must first consider the tumor site; in fact, infectious complications are more frequent in the oral cavity/oropharynx, while at the level of hypopharynx/larynx there was an higher frequency by reconstructive techniques. There were not infections in the case of parotid surgery or neck dissections.

Among underlying diseases, infections frequently occurred in patients affected by chronic obstructive pulmonary disease in case of oral cavity/oropharynx tumors and diabetics/kidney disease patients in case of hypopharynx/larynx tumors.

In agreement with the literature, histology, and tumor extent, associated with malnutrition patient, are worsening factors of postoperative hospital stay.

Regarding therapy, some drugs have been less effective to prevent post-operative infection: the ceftriaxone at the level of the oral cavity/oropharynx and ceftriaxone/pefloxacin at the level of the hypopharynx/larynx.

Instead, the imipenem/cilastatin, the pefloxacin and teicoplanin were more effective to hold the eradication of the infection and the recurrence of the same at the level of the hypopharynx/larynx.

We haven't derived resolute data for the oral cavity/oropharynx, probably due to the small number of patients. The pre-operative prophylaxis has been practiced in 33% (3/9, mean 1 day) of patients with oral cavity/oropharynx tumors and in 21.4% (22/103, mean of 2 days) of patients with hypopharynx/larynx neoplasms.

Despite the pre-operative prophylaxis, 100% (3/3) of patients affected by oral cavity/oropharynx tumors and 45.4% (10/22) of patients with hypopharynx/larynx cancers developed infectious complications.

In conclusion we believe on the major efficacy of peri-operative prophylaxis in the case of clean/contaminated interventions of the head/neck surgery respect to the pre-operative prophylaxis.

The peri-operative prophylaxis should be started immediately before anesthetic procedures and, if necessary, whether the intervention is still in progress, with an intra-operative dose after a time from the beginning of the intervention of twice the used drug's half-life.

Riassunto

Le infezioni post-operatorie nella chirurgia oncologica possono compromettere non solo l'esito chirurgico ma anche essere responsabili di ritardi per eventuali trattamenti adiuvanti. I rischi di infezioni postoperatorie nella chirurgia del cancro della testa-collo scendono dal 30-80% al 20% con la profilassi antibiotica perioperatoria. Nonostante l'introduzione, come da linee guida, della profilassi preoperatoria, il numero di infezioni post-chirurgiche rimane ancora elevato (40/61% dei casi). È importante conoscere i fattori di rischio intrinseci (legati al paziente) ed estrinseci (legati all'ambiente esterno e alla stessa procedura) per capire meglio come prevenire le infezioni. Il ricovero prolungato può esporre i pazienti al rischio di agenti patogeni ospedalieri. Nel nostro lavoro abbiamo considerato le problematiche legate al ricovero post-operatorio nei pazienti degenti presso il nostro reparto ORL negli ultimi 4 anni. Abbiamo cercato di delineare un profilo di pazienti con carcinoma del distretto testa-collo che hanno maggiori probabilità di contrarre infezioni post-operatorie. Abbiamo anche confrontato gli effetti di vari antibiotici somministrati prima e dopo l'insorgenza delle complicanze per suggerire un protocollo terapeutico.

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