Do Italian surgeons use antibiotic prophylaxis in thyroid surgery?
Results from a national study (UEC – Italian Endocrine Surgery Units Association)

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Do Italian surgeons use antibiotic prophylaxis in thyroid surgery? Results from a national study (UEC – Italian Endocrine Surgery Units Association)

Thyroid surgery is a clean procedure and therefore antibiotic prophylaxis is not routinely recommended by most international guidelines. However, antibiotics are often used in clinical practice. We enrolled 2926 patients who performed a thyroid surgical operation between the years 2009 and 2011 in the 38 centers of endocrine surgery that joined the UEC – Italian Endocrine Surgery Units Association.
Antibiotic prophylaxis was used in 1132 interventions (38.7%). In case of antibiotic prophylaxis, cephalosporins or aminopenicillins ± beta lactamase inhibitors were employed. At logistic regression analysis the use of drainage or device and the presence of malignancy were independent predictors of antibiotic prophylaxis employment.
In conclusion our study shows that antibiotic prophylaxis was not rarely used in clinical practice in the setting of thyroid surgery. Drainage apposition, use of device, and malignant disease were independent predictors for antibiotic prophylaxis employment. More data on everyday practice and infection rate in well-designed studies are warranted to provide definitive recommendations on the utility of antibiotic prophylaxis in this setting.
According to our experience, we don't consider to be strictly necessary the antibiotic prophylaxis employment in order to reduce infection rate in thyroid surgery.

KEY WORDS: Antibiotic prophylaxis, Drainage, Malignancy, Resistance, Thyroid surgery

Introduction

Would infection rate in the setting of thyroid surgery is extremely low (0.3-0.6%) [1-3]. For this reason thyroid surgery is considered a clean procedure and antibiotic prophylaxis is not routinely recommended by most international guidelines.

However, according to the few studies available on this topic, antibiotics are used in clinical practice by about 50% of surgeons [1,2]. Therefore a conflict seems to exist between what is recommended and what happens in reality.
Italian Endocrine Surgery Units Association UEC performed a study devoted to detection of complications rate in patients who underwent thyroid surgery between 2009 and 2011 in the 38 centers of endocrine surgery that participated to the study.
In the present sub-analysis we used data of this study that concern the employment of antibiotic prophylaxis.
Aim of the present study is to show the rate of antibiotic prophylaxis employment in clinical practice and the factors that are associated with its use.

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Patients and methods

A website was created to the aim of entering patients data. Each center received a personal password to enter the website.
All patients who underwent thyroid surgery regardless of the diseases were enrolled.
We recorded age, sex, type of intervention, use of device or drainage, type of disease and surgeons experience (in terms of interventions per year).
We recorded use of antibiotic prophylaxis and consider this as the dependent variable.

STATISTICAL ANALYSIS

The Kolmogorov-Smirnov test was used to check quantitative variables for Gaussian distribution. In case of Gaussian distribution, data are reported as mean ± standard deviation (SD), while in case of non-Gaussian distribution they are reported as median and interquartile range (IQR). In case of Gaussian distribution, the Student's t-test for unpaired variables was applied, while the Mann-Whitney U was used in case of non-Gaussian distribution. The ^{2} test with Yates correction (or Fisher's exact test where appropriate) was used for categorical variables. A $p < 0.05$ at two-sided test was considered statistically significant. Any independent variable statistically different in the two groups (using or not antibiotic prophylaxis) or with a $p \leq 0.2$ at univariate analysis was included in binary logistic regression analysis using the forward conditional stepwise method. The cut-off values used for the stepwise method were: $p=0.05$ for entry into the model and $p=0.10$ for its removal. All statistical analyses were carried out using the Statistical Package for the Social Sciences version 18.0 (SPSS Inc. Chicago, III).

Results

We enrolled 2926 patients who performed a thyroid surgical operation between the years 2009 and 2011 in the 38 centers of endocrine surgery that joined the UEC.
Mean demographic and clinical data are listed in table I.
Most interventions were performed by high-experienced surgeons: 50.5% of surgeons declared to have performed more than 100 interventions per year; 15.4% declared 100 interventions per year; 12.9 declared 75 interventions per year; 8.7% declared 50 interventions per year; 7.5% declared 25 interventions per year and only 2.4% declared less than 25 interventions per year.
Antibiotic prophylaxis was used in 1132 interventions (38.7%). Most used antibiotics were cephalosporins or aminopenicillins ± beta lactamase inhibitors.
Table II shows the demographic and clinical variables of the patients stratified according to the presence/absence of antibiotic prophylaxis and the results of univariate analysis.
We categorized numbers of interventions using 100 per years as the cutoff (1402 performed more than 100 interventions per year and 1373 less or equal to 100 interventions per year). According to this categorization, surgeons with more than 100 interventions per year tended to use less frequently antibiotic prophylaxis than less experienced surgeons (35.7% vs. 38.6%, p=0.109), even though this difference did not reach statistical significance.
At logistic regression analysis the use of drainage or device and presence of malignancy were independent predictors of antibiotic prophylaxis employment whereas surgeon's experience was not (Table III).

TABLE I - *Demographic and clinical data of the patients (n= 2926)*

Age (years)	52 ± 14.6
Sex	
M	22.3%
F	77.7%
Type of intervention	
Total/near total thyroidectomy	89.9%
Loboistemctomy	10.1%
Use of any device	80%
Use of drainage	91.4%
Malignancy	14.7%
Disease	
Multinodular euthyroid goiter	39.3%
Papillifer carcinoma	11.9%
Single nodule	11.3%
Cervico-mediastinal goiter	9.1%
Multinodular toxic goiter	8.0%
Graves's diseases	5.1%
Follicular adenoma	4.0%
Hashimoto disease	3.3%
Relapsed goiter	2.9%
Plummer disease	2.1%
Follicular carcinoma	1.6%
Medullary carcinoma	0.8%
Anaplastic carcinoma	0.3%
Thyroid cyst	0.3%

Some percentages do not add up to 100% because of rounding. Data are reported in percentage for categorical variables and mean ± standard deviation for quantitative variables

Discussion

Thyroid surgery is the main therapeutical option for thyroid cancer [4].
Detection of BRAF mutation before surgery is recommended as a useful diagnostic marker and prognostic indicator for papillary thyroid carcinoma (PTC), and

Table II - *Demographic and clinical features of the patients and operator experience stratified by presence or absence of antibiotic prophylaxis (n= 2926)*

Variable	Patients who received antibiotic prophylaxis (n=1132)	Patients who did not receive antibiotic prophylaxis (n= 1794)	P
Age (years)	52 ± 14.8	52 ± 14.5	0.958
Sex			0.373
M	23.1%	21.7%	
F	76.9%	78.3%	
Type of intervention			0.603
Total/near total thyroidectomy	90.3%	89.7%	
Loboistemctomy	9.7%	10.3%	
Use of any device	88.8%	74.5%	<0.001
Use of drainage	93.2%	90.3%	0.006
Malignancy	19.6%	11.5%	<0.001
Disease			<0.001
Multinodular euthyroid goiter	40.6%	38.4%	
Papillifer carcinoma	16.7%	8.9%	
Single nodule	12.5%	10.5%	
Cervico-mediastinal goiter	7.2%	10.2%	
Multinodular toxic goiter	7.2%	8.5%	
Graves's diseases	3.7%	6.0%	
Follicular adenoma	2.8%	4.7%	
Hashimoto disease	2.4%	3.9%	
Relapsed goiter	2.5%	3.2%	
Plummer disease	1.1%	2.7%	
Follicular carcinoma	1.7%	1.6%	
Medullary carcinoma	0.9%	0.8%	
Anaplastic carcinoma	0.4%	0.3%	
Thyroid cyst	0.4%	0.3%	

Some percentages do not add up to 100% because of rounding. Data are reported in percentage for categorical variables and mean ± standard deviation for quantitative variables

Table III - *Logistic regression analysis for the use of antibiotic prophylaxis*

	Regression coefficient	Standard Error	OR (95% CI)	P
Use of drainage	1.424	0.210	4.154 (2.753-6.268)	<0.001
Use of device	0.938	0.111	2.556 (2.057- 3.175)	<0.001
Malignancy	0.560	0.112	1.751 (1.405-2.182)	<0.001
Surgeon's experience (>100 interventions yearly)	-0.097	0.081	0.907 (0.774-1.063)	0.229

thus influences surgeon's decision on management of PTC [5]. Furthermore, predominant internal flow seen on color Doppler ultrasonography is associated with malignancy of thyroid in thyroid follicular neoplasms (FN). Absence of internal flow or predominantly peripheral flow indicates a low probability of thyroid FN malignancy [6,7].

Thyroid surgery is considered clean surgery, because of a very low rate of infections (0.3-0.6%), even though an older study report a little bit higher figures (2.65%) [8]. The aesthetic results of thyroidectomy have been also evaluated in an Italian prospective single-blinded randomized study [9]. Keloid scars are rare complications in thyroid surgery and are the result of a dysregulated process of wound healing, with proliferation of scar tissue beyond the boundaries of the inciting wound; medical.therapy is still disappointing [10]. Due to this very low risk, thyroid surgery should not require an antibi-

otic prophylaxis and this is corroborated by most scientific society guidelines. In contrast, the few data available in everyday practice indicated that antibiotic prophylaxis is not rarely employed by the surgeons.
Our study shows that antibiotic prophylaxis was used in 38.7% of thyroid interventions. This figure is lower than observed in a previous multicentric study [1,2], but remains very high considering that thyroid surgery is a clean and therefore a low-risk infection surgery. In a survey carried out in United Kingdom, the rate of antibiotic prophylaxis employment resulted to be much lower. In fact antibiotic prophylaxis was administered routinely in only 9% of patients, and in 16% of selected cases while 75% of patients did not receive the prophylaxis [11]. The Scottish Intercollegiate Guidelines network (SIGN) does not advocate routine antibiotic prophylaxis for benign pathologies but only in selected cases of malignancies [12].
Moreover a randomized controlled trial carried out in Italy showed no benefit of antibiotic prophylaxis in the setting of thyroid surgery[1]. However, we underline that only subjects aged less than 80, without metabolic diseases (such as diabetes mellitus) and without an aspirating drain were enrolled in that trial [1,2].
We acknowledge that a potential limitation of our study is the lack of information regarding comorbidities that could be associated with a higher infective risk and therefore with a higher use of antibiotic prophylaxis. However, it is noteworthy that age, that is one of the variables most related to comorbidities, is not different in patients who received and who did not receive antibiotic prophylaxis.
We underline that an unnecessary antibiotic prophylaxis carries several issues:
– the potential selection of nosocomial resistant strains due to massive use of antibiotics;
– the potential toxicity of antibiotics that, as all the drugs, have the potential to be harmful for the patient (e.g. allergic reactions);
– the cost of the drugs and the cost related to the potential complications indicated above.
In other words all that is unnecessary may be detrimental for the patient.
Our study shows that the employment of antibiotic prophylaxis was more common in patients in whom a drain has been positioned, a device has been used or a malignancy was present. This is related to the perception of infective risk by the surgeon but not necessarily with the actual infective risk.
In fact a systematic review failed to evidence a higher risk of infection when a drainage is used in thyroid surgery [13].
In conclusion our study shows that antibiotic prophylaxis was used in 38.7% of thyroid interventions in Italy. Drainage apposition, use of device, and malignant disease were independent predictors of antibiotic prophylaxis employment. Data on everyday practice and infection rate in well-designed studies are needed to provide definitive recommendations on the utility of antibiotic prophylaxis in this setting.
According to our experience [1,2]., we don't consider to be strictly necessary the antibiotic prophylaxis employment in order to reduce infection rate in thyroid surgery.

Riassunto

La chirurgia tiroidea è una chirurgia pulita e pertanto la profilassi antibiotica non è raccomandata di routine dalla gran parte delle linee guida internazionali. Tuttavia, gli antibiotici sono spesso usati nella pratica clinica. Dal 2009 al 2011 abbiamo arruolato 2926 pazienti sottoposti a chirurgia della tiroide in 38 centri di chirurgia endocrina della UEC, l'Associazione delle Unità di Endocrinochirurgia Italiane.
L'antibioticoprofilassi è stata praticata in 1132 interventi (38,7%). Quando praticata, sono state utilizzate le cefalosporine o le aminopenicilline ± gli inibitori delle betalattamasi. All'analisi della regressione logistica l'utilizzo del drenaggio, l'uso di un device e la presenza di patologia maligna, sono risultati essere fattori predittivi indipendenti per l'impiego dell'antibioticoprofilassi.
In conclusione il nostro studio mostra che l'antibioticoprofilassi nell'ambito della chirurgia tiroidea non è stata utilizzata di rado nella pratica clinica. Il posizionamento di un drenaggio, l'uso di un device, la patologia maligna sono fattori predittivi indipendenti per l'impiego dell'antibioticoprofilassi.
È necessario raccogliere un maggior numero di dati attraverso studi programmati sulla pratica clinica e sui tassi di infezione al fine di fornire raccomandazioni definitive sull'utilità dell'antibioticoprofillassi in chirurgia tiroidea.
Secondo la nostra esperienza l'antibioticoprofilassi non riduce il tasso di infezioni in chirurgia tiroidea.

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