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MISCELLANEOUS

Prophylactic antibiotics in sialendoscopy: a randomized clinical trial

Carlos M. Chiesa-Estomba[1,3,9] · Alvaro Sanchez-Barrueco[2,4] · Giovanni Cammaroto[5,9] · Jerome R. Lechien[6,8] · Miguel Mayo-Yanez[7,8] · Carlos Cenjor[2,4] · Pasquale Capaccio[8,9] · Carlos Saga-Gutierrez[1]

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Abstract

Objective Antibiotics have been prescribed routinely in sialendoscopy procedures to reduce the risk of postoperative infection, despite the limited evidence supporting this practice. Being necessary to assess the need for antibiotics in Sialendoscopy, aiming to provide evidence-based guidance to clinicians regarding antibiotic administration in this procedure.

Materials & method A prospective, randomized, double-blind, controlled clinical trial to evaluate the of prophylactic antibiotics in Sialendoscopy was designed.

Results A total of 80 patients were included in this study, including 57 females (71.8%) and 23 males (28.8%). In terms of prophylaxis, 36 patients (45%) received prophylactic treatment, and 44 patients (55%) did not. The occurrence of infectious events was observed in 2 patients (5.6%) with prophylaxis and 4 patients (9.1%) without prophylaxis. However, this difference was not statistically significant ($p = 0.556$).

Conclusion In conclusion, our prospective, randomized clinical trial aimed to address the debate regarding the use of prophylactic antibiotics in sialendoscopy. Our study's findings suggest that the routine use antibiotics may not be necessary to prevent postoperative infections in sialendoscopy procedures. These results have important implications for clinical practice, potentially reducing the unnecessary use of antibiotics and addressing concerns related to antibiotic resistance and adverse drug reactions.

Keywords Sialendoscopy · Antibiotics · Prophylaxis

✉ Carlos M. Chiesa-Estomba
chiesaestomba86@gmail.com

[1] Department of Otorhinolaryngology, Osakidetza Donostia University Hospital, Biodonostia Research Institute, San Sebastian 20014, Spain

[2] ENT and Cervicofacial Surgery Department, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

[3] Otorhinolaryngology Department, Faculty of Medicine, Deusto University, Bizkaia, Spain

[4] Otorhinolaryngology Department, Faculty of Medicine, Universidad Alfonso X el Sabio, Madrid, Spain

[5] Department of Head-Neck Surgery, Otolaryngology, Head-Neck and Oral Surgery Unit, Morgagni Pierantoni Hospital, Forlì 47121, Italy

[6] Department of Otolaryngology and Head and Neck Surgery, Division of Laryngology and Broncho-Esophagology, UMONS Research Institute for Health Sciences and Technology, EpiCURA Hospital, University of Mons, Mons, Belgium

[7] Otorhinolaryngology - Head and Neck Surgery Department, Complexo Hospitalario Universitario A Coruña (CHUAC), Galicia 15006, A Coruña, Spain

[8] Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

[9] Head & Neck Study Group of Young-Otolaryngologists of the International Federations of Oto-rhino-laryngological Societies (YO-IFOS), Paris, France

Introduction

Sialendoscopy represents a minimally invasive diagnostic and therapeutic procedure for salivary gland disorders. This approach that has gained increasing recognition as a valuable tool in the diagnosis and management of various salivary obstructive disorders over the past few decades [1]. Certainly, this endoscopic technique has revolutionized the field of salivary gland surgery, offering a less invasive alternative to traditional open surgical procedures [1], enabling surgeons to both the visualization and treatment of salivary gland ductal pathologies, such as sialolithiasis and strictures, with reduced morbidity and improved patient outcomes [2, 3].

While the benefits of sialendoscopy are well-documented, some aspects of the procedure remain subjects of debate within the medical community. One such topic is the administration of prophylactic antibiotics during sialendoscopy. Antibiotic usage in surgical and endoscopic procedures has been a longstanding practice aimed at preventing postoperative infections. However, the necessity of antibiotics in sialendoscopy remains a controversial issue, due to the lack of evidence and the varied clinical practices among otolaryngologists and oral and maxillofacial surgeons.

Antibiotics have been prescribed routinely in sialendoscopy procedures to reduce the risk of postoperative infection, despite the limited evidence supporting this practice. Moreover, antibiotic overuse and the associated concerns of antibiotic resistance and adverse drug reactions underscore the importance of revisiting the need for prophylactic antibiotics in sialendoscopy [4–6].

In this study the authors conducted a controlled randomized clinical trial aimed to assess the need for antibiotics in Sialendoscopy, aiming to provide evidence-based guidance to clinicians regarding antibiotic administration in this procedure.

Methods

Study design

A prospective, randomized, double-blind, controlled clinical trial was designed to compare the use of prophylactic antibiotics in sialendoscopy (Prophylactic Amoxicillin/Clavulanic acid 1gr.). The trial was conducted in 4 different Tertiary University Hospital between January the 15th of 2022 and January the 15th of 2023. Approval from the Basque Country Institutional Review Board (IRB) was confirmed (CHI-SIA-2020-01). The study was run in compliance with ethical standards outlined in the Declaration of Helsinki. Written informed consent will be obtained from all participants before their enrollment. (Fig. 1)

Participants

Inclusion criteria

Adult patients (age ≥ 18 years) scheduled to undergo sialendoscopy for different salivary gland ductal pathologies, including sialolithiasis (3 mm or less in the submandibular

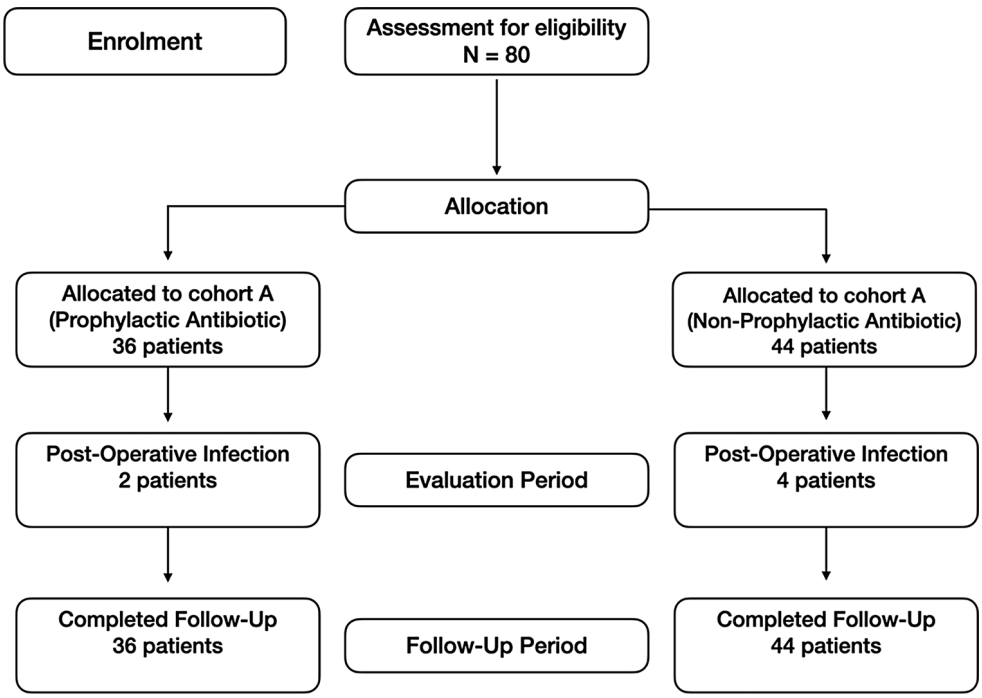

Fig. 1 Study Flow-Diagram

and the parotid gland) and strictures. Patients willing and able to provide informed consent.

Exclusion criteria

Patients with a known allergy or hypersensitivity to the study antibiotics; or patients with a previous history of chronic salivary gland infections or individuals currently on antibiotic therapy for unrelated conditions. Also immunocompromised patients, and pregnant or lactating individuals were excluded. Any type of combined approach that included a mucosal incision and/or mucosal suture was excluded, such as papillotomy, transoral or transfacial combined approaches.

Randomization and blinding

This clinical trial was registered under the registration number EudraCT 2020-005824-12 at the Spanish Agency for Medicines and Health Products (AEMPS). Patients meeting the inclusion criteria were randomly assigned to one of two study arms: the antibiotic group or the placebo group. Randomization was achieved through computer-generated random numbers, and allocation was concealed. (Fig. 1) Both participants and healthcare providers involved in the sialendoscopy procedure were blinded to the group assignment. The blinding code was maintained by an independent third party until the completion of data analysis. (Consort Checklist – Supplementary material).

Intervention

Antibiotic group

Patients in this group received a single preoperative dose of Amoxicillin/Clavulanic Acid 1gr, 30 min before sialendoscopy as prophylaxis, intravenously.

Control group

Patients in this group didn´t receive any kind of treatment.

Sialendoscopy procedure

All sialendoscopy procedures were performed by experienced otolaryngologists following standard protocols. All procedures were carried out under general or local anesthesia according with patients and surgeon preference. After progressive dilatation of the submandibular or parotid main duct caruncle (Marchal Dilator Set, Karl Storz Co., GmbH, Tuttlingen, Germany), a sialendoscopic evaluation of the ductal system was performed using a 0.8 mm and 1.1 mm (Erlangen Sialendoscope®, Karl Storz Co., GmbH, Tuttlingen, Germany) as well as 1.3 mm optic (Marchal All-in-one sialoendoscope®, Karl Storz Co., GmbH, Tuttlingen, Germany). The duration of the procedure will remain consistent across both study groups. In case of ductal stricture dilation or lack of papilla distensibility, after ductal dilation, a ductal stent was placed and removed after at least 2 weeks. In case of sialolithiasis, extraction was performed using Dormia Basket (Karl Storz Co., GmbH, Tuttlingen, Germany) or NGage Basket (Cook Group Co., Bloomington, United States).

Outcome measures

The primary outcome was to investigate the incidence of postoperative infections, including sialadenitis and wound infection, within 30 days of the sialendoscopy procedure. Relevant secondary outcomes were collected like: postoperative pain, length of hospital stay, if applicable; need for additional interventions (e.g., postoperative antibiotics, drainage, or surgical revision); adverse drug reactions or complications within 30 days of the procedure. Patients where follow-up during at least 6 months after the surgical procedure.

Statistical analysis

Data was analyzed using appropriate statistical methods, including chi-square tests, t-tests, or non-parametric equivalents, as appropriate. p-values < 0.05 was considered statistically significant. A power analysis was conducted to determine the required sample size based on the expected effect size and significance level, being at least 25 patients on each arm necessary to obtain a power of 80% to detect an effect size of 0.809. Data was collected and managed using a secure electronic database. An independent Data Monitoring Committee will overseed the trial's progress and data integrity.

Ethical considerations

The study will adhere to ethical guidelines, and patient confidentiality was strictly maintained throughout the trial.

Informed consent

Written informed consent was obtained from all participants prior to enrollment, and they were made aware of their right to withdraw from the study at any time without affecting their medical care.

Results

A total of 80 patients were included in this study, including 57 females (71.8%) and 23 males (28.8%) ($p=0.237$). The mean age of the participants was 52 +/- 14 years (Min: 18/Max: 79). Regarding comorbidities, 25 patients (31.3%) had arterial hypertension (AHT), 3 patients (3.8%) had hyperuricemia, and 7 patients (8.8%) had diabetes mellitus (DM).

Table 1 Demographic variables and comparison

Variables	*N* (PG) 36 patients	*N* (NPG) 44 patients	Total (%)	*p*
Sex	23	34	57 (71.8)	0.237
Female	13	10	23 (28.8)	
Male				
Age	52 +/- 14 (Min: 18/Max: 79)	49 +/- 11 (Min: 18/Max: 74)		0.500
AHT	11	14	25 (31.3)	0.429
Hyperuricemia	1	2	3 (3.8)	1.000
DM	3	4	7 (8.8)	0.482
Diagnosis	8	5	13 (16.3)	0.310
Sialolithiasis	6	13	19 (23.8)	
Sialadenitis	10	13	23 (35)	
Duct Stricture	2	7	9 (11.3)	
Iodine Radio-	4	4	8 (10)	
Induced sialadenitis	1	2	3 (3.8)	
Lack of papilla distensibility				
Mucus Plug				
Previous episodes of inflammation	0.5 +/- 0.9 (Min: 0/Max: 5)	0.7 +/- 1.1 (Min: 0/Max: 6)		0.864
Years of evolution	3 years +/- 3 (Min: 1/Max: 11)	3.1 years +/- 5 (Min: 1/Max: 20)		0.973
Gland affected.	22	28	50 (62.5)	0.596
Parotid gland	11	11	22 (27.5)	
Submandibular gland	3	5	8 (10)	
Parotid & Submandibular gland				
Side affected.	18	17	35 (43.8)	0,781
Left	11	19	30 (37.5)	
Right	7	8	15 (18.8)	
Bilateral				
Complications	0	1	1 (1,25)	0.540
Ductal perforation	1	0	1 (1,25)	
Oedema.	2	2	4 (5)	
Pain				
Intraductal corticoid	33	38	71 (88.8)	
Yes	3	6	9 (11.3)	
No				
Surgical time	45 min +/- 15 (Min: 18/Max: 86)	49 min +/- 16 (Min: 20/Max: 79)		0.548
Procedure success	35	42	77 (96.3)	
Yes	1	2	3 (3.7)	
No				

None of these comorbidities showed statistically significant associations with post-operative outcome. (Table 1)

The most common primary diagnoses among the patients were ductal stricture or stenosis (23 patients, 35%), sialadenitis secondary to a Sjögren Syndrome (19 patients, 23.8%), and sialolithiasis (13 patients, 16.3%). Other less common diagnoses included iodine radio-induced sialadenitis (9 patients, 11.3%), lack of papilla distensibility (10 patients, 12.5%), and mucus plug (3 patients, 3.8%). The distribution of these diagnoses did not yield statistically significant differences ($p=0.310$). (Table 1)

Regarding the gland affected, the parotid gland was affected in 50 patients (62.5%), the submandibular gland in 22 patients (27.5%), and both the parotid and submandibular glands in 8 patients (10%). No statistically significant differences were observed based on the gland affected ($p=0.596$). Regarding side affected, 35 patients (43.8%) had left-sided involvement, 30 patients (37.5%) had right-sided involvement, and 15 patients (18.8%) had bilateral involvement. The distribution of side affected did not show statistical significance ($p=0.781$). Peri-operative complications such as ductal perforation, edema, were reported in 1 patient each and post-operative pain was reported in 4 (5%) cases. The occurrence of complications did not demonstrate statistical significance ($p=0.540$). (Table 1) The procedure was successful in 77 patients (96.3%), while 3 patients (3.7%) experienced treatment failure.

In terms of prophylaxis, 36 patients (45%) received prophylactic treatment, and 44 patients (55%) did not. The occurrence of infectious events was observed in 2 patients (5.6%) with prophylaxis and 4 patients (9.1%) without prophylaxis. However, this difference was not statistically significant ($p=0.556$). Three of the 6 cases of infection were secondary to a sialendoscopy procedure in patients with a ductal stricture. All the patients were diagnosed in the first week after the procedure, in 2 cases a CT-Scan was performed for evaluation. In all the cases, the diagnosis was performed in the ENT clinic of the departments involved (Fig. 2). The six patients receive antibiotics treatment to treat the infection. Regarding the gland affected, in four cases, the gland affected was the parotid gland and in 2 of them the submandibular gland. Just 1 patient suffer from Sjögren Syndrome, the other 5 don't have any comorbidities. No patient required surgical drainage, hospitalization or suffer from adverse drug reactions. (Table 2)

Discussion

The primary objective of the present study was to assess the need for prophylactic antibiotics in sialendoscopy. The results obtained revealed that the occurrence of infectious

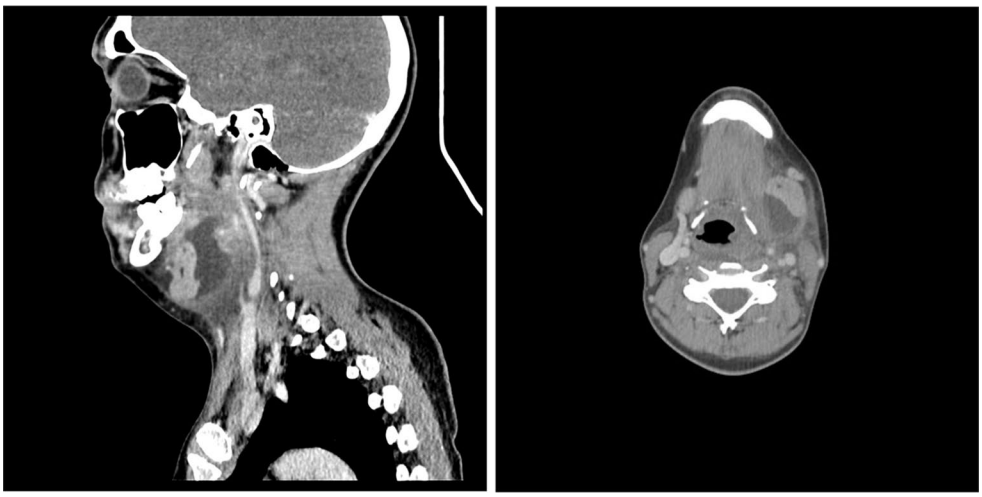

Fig. 2 CT-Scan of a patient with a submandibular abscess secondary to a sialendoscopy procedure

Table 2 Comparison regarding infectious events among patients with and without prophylaxis

Variables	*N* (Infections)	%	*p*
Prophylaxis			
Yes	36 (2)	45	0.556
No	44 (4)	55	

events did not significantly differ between patients' groups. This finding challenges the routine use of antibiotics in sialendoscopy, suggesting that their prophylactic administration may not provide a significant benefit in preventing postoperative infections.

Sialendoscopy has been proven to be a safe and cost-effective alternative technique, useful to avoid complications associated with classical sialadenectomy [7, 8]. In general, the efficacy of the technique alleviating patients' symptoms ranges from 85 to 98%, generating an increasing interest in this procedure worldwide [9–12]. Our results (92% success) corroborate success rates described in the literature. Moreover, the occurrence of adverse events is uncommon and results from the technique have demonstrated long-term efficacy, with high patient satisfaction rates even after 6 years of the procedure [13].

Post-operative infections in sialendoscopy is relative rare. In our study 6 (7.5%) patients experienced a post-operative infection. Results were slightly higher than those reported in the literature by authors like Karagozoglu et al. [14] with 3.8% or Jokela et al.[15]who reported infection rates after Sialendoscopy of 6.4%.* Notably, in our series, post-operative infection was more common in patients affected by ductal stenosis. Something that can be explained by the study design, where combined approaches were excluded; hence the main obstructive pathologies treated were strictures, sialadenitis, floating < 3 mm stones, lack of papilla distensibility, and mucus plug. A subset of pathologies usually related to salivary fluid ectasia, and where the potential introduction of pathogens during ductal manipulation can increase the risk of infection.

On the other side, antimicrobial resistance represents a worldwide threat, and it´s associated with almost 700.000 deaths per year [16]. The increased dissemination of resistant bacteria turning this into one of the most relevant public health threats in the 21st century forcing organizations to take urgent action.[17, 18] Therefore, the indiscriminate use of antibiotics it will be associated with increased costs and risks to patients like antibiotic-resistant bacteria [4, 5]. This is of concern if widening resistance renders available antibiotics ineffective, in addition to commonly cited side effects [6]. In this vein, looks necessary to improve the rational use of antibiotics in Otorhinolaryngology and Head and Neck surgery.[18].

Furthermore, it is important to emphasize that antibiotic prophylaxis cannot compensate for incorrect surgical safety protocols. Hand scrub, correct handling of the surgical site, a clean environment in the operating room and decontamination of medical devices and surgical instruments, careful management of surgical instruments during surgery as well as a proper surgical technique to minimize the duration of surgery are all crucial factors to avoid potential infections.

Our study has some limitations. Patients were treated in tertiary centers, which are referral clinics for these procedures. Additionally, the study was conducted in a controlled clinical trial setting, and results may not fully capture real-world clinical practice variations.

Conclusion

In conclusion, our prospective, randomized clinical trial aimed to address the debate regarding the use of prophylactic antibiotics in sialendoscopy. Our study's findings suggest that the routine use antibiotics may not be necessary

to prevent postoperative infections in sialendoscopy procedures. These results have important implications for clinical practice, potentially reducing the unnecessary use of antibiotics and addressing concerns related to antibiotic resistance and adverse drug reactions. Future research with larger cohorts and multicenter studies should further explore the role of antibiotics in sialendoscopy, considering different patient populations and salivary gland pathologies. Ultimately, evidence-based guidelines can help clinicians make informed decisions about the use of antibiotics in sialendoscopy, optimizing patient care while minimizing unnecessary antibiotic exposure.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00405-024-08773-z.

Author contributions Carlos M. Chiesa-Estomba: study design, patient recruitment, data collection, manuscript drafting. Alvaro Sanchez-Barrueco: patient recruitment, data collection. Giovanni Cammaroto: patient recruitment, data collection. Jerome R. Lechien: data curation, statistical analysis, manuscript revision. Miguel Mayo-Yanez: data curation, statistical analysis, manuscript revision. Carlos Cenjor: patient recruitment, data collection. Salvatore, Capaccio: study desing, manuscript drafting. Carlos Saga-Gutierrez: patient recruitment, data collection, manuscript drafting.

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