Multinational Comparison of Prophylactic Antibiotic Use for Eyelid Surgery

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IMPORTANCE Antibiotic stewardship is important in controlling resistance, adverse reactions, and cost. The literature regarding antibiotic use for eyelid surgery is lacking.

OBJECTIVES To determine standard care and assess factors influencing antibiotic prescribing practices for eyelid surgery.

DESIGN, SETTING, AND PARTICIPANTS A survey study was conducted from February 2, 2014, to March 24, 2014. The survey was distributed to 2397 oculoplastic surgeons in private and academic oculoplastic surgery practices in 43 countries. All surgeons were members of ophthalmic plastic and reconstructive surgery societies. Data were analyzed by geographic location. Linear regression was performed to quantify contributions to rates of prescribing postoperative antibiotics for routine eyelid surgical procedures.

MAIN OUTCOMES AND MEASURES Rates of prescribing prophylactic intravenous, oral, and topical antibiotics as well as factors that influence surgeons’ prescribing practices.

RESULTS A total of 782 responses were received from 2397 surgeons (average response rate, 36.7%; 2.5% margin of error) from 43 countries. Topical antibiotic use was common in all regions (85.2%). Perioperative intravenous antibiotic use was uncommon in all regions (13.5%). Geographic location was the greatest predictor of antibiotic prescribing practices (range, 2.9% in the United Kingdom to 86.7% in India; mean, 24%). Within Europe, Italy had the highest rate of antibiotic prescriptions for eyelid surgery (41.7%) and the United Kingdom had the lowest rate (2.9%). In South America, Venezuela had the highest rate of antibiotic prescriptions for eyelid surgery (83.3%) and Chile had the lowest rate (0%). The practice locations that were associated with routinely prescribing postoperative oral antibiotics were India (odds ratio [OR], 15.83; 95% CI, 4.85-51.68; \( P < .001 \)), Venezuela (OR, 13.47; 95% CI, 1.43-12719; \( P = .02 \)), and Southeast Asia (OR, 2.80; 95% CI, 1.15-6.84; \( P = .02 \)). Conversely, practice location in the United Kingdom (OR, 0.048; 95% CI, 0.0063-0.37; \( P = .004 \)), Australia and New Zealand (OR, 0.15; 95% CI, 0.033-0.67; \( P = .01 \)), and the United States and Canada (OR, 0.41; 95% CI, 0.23-0.72; \( P = .002 \)) were associated with decreased rates of postoperative oral antibiotic use. Surgeons’ concern for allergic reactions was associated with decreased rates of prescribing antibiotics (OR, 0.34; 95% CI, 0.23-0.49; \( P < .001 \)), while surgeons’ concern for infection was associated with increased rates of prescribing antibiotics (OR 1.80; 95% CI, 1.45-2.23; \( P < .001 \)).

CONCLUSIONS AND RELEVANCE These results from members of ophthalmic plastic and reconstructive surgery societies confirm that antibiotic prescribing practices for routine eyelid surgical procedures vary widely throughout the world. No standard of care has been established that would require the routine use of postoperative prophylactic antibiotics following eyelid surgery.

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At a 2009 meeting of the New England Oculoplastics Society, members contemplated the contentious matter of when and in what circumstances antibiotics should be prescribed in the treatment or prophylaxis of orbital infection. That animated debate spawned a retrospective multicenter review of nearly 700 cases to assess the role of prophylactic postoperative antibiotics in representative orbital surgery. No advantage was identified to support their use. When the matter was revisited at the 2013 meeting of the European Society of Ophthalmic Plastic and Reconstructive Surgery in Barcelona, prescribing patterns among attendees appeared wildly divergent despite the data presented. Facing purely speculative explanations for the perceived regional differences, the present survey was conceived.

The use of antibiotics in medicine, industry, and society has come under increasing scrutiny. Frequently cited issues are increased antibiotic resistance among bacteria, allergic reactions of varying severity, and cost. Less-well publicized issues are antibiotic-induced neurotoxicity, mitochondrial dysfunction, obesity, airway dysfunction, and pro-tein un-intentional effects from manipulation of the microbiome. Government agencies in the United States and Europe have lobbied strongly for abstinence from anti-biotics to identify and assess factors influencing the antibiotic prescrib-ing practices of oculoplastic surgeons. A complete list of questions is included in the box. As can be seen, factors assessed included practice location, clinical setting (hospital-based or private practice), perceived infection rates, and adverse event rates. In addition, questions were included to assess the use of intravenous, oral, and topical antibiotics in the perioperative period.

Content and wording of questions were developed by a panel of oculoplastic surgeons (F.B., M.H.D., A.F., D.M., N.N., T.H.O., and E.J.W.). Questions regarding practice and training location were customized for each region of the world to which the survey was distributed. All other questions were identical across all regions. Questions were translated into the standard language for professional communication in each region by native speakers from within the study group.

### Methods

#### Survey Design

To examine antibiotic prescribing practices worldwide in oculoplastic surgical procedures, a survey was developed through the collaborative efforts of a multinational study group. This survey study was conducted from February 2, 2014, to March 24, 2014. The primary aim of the survey was to identify and assess factors influencing the antibiotic prescribing practices of oculoplastic surgeons. A complete list of questions is included in the box. As can be seen, factors assessed included practice location, clinical setting (hospital-based or private practice), perceived infection rates, and adverse event rates. In addition, questions were included to assess the use of intravenous, oral, and topical antibiotics in the perioperative period.

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#### Survey Deployment

To ensure sufficient reach of the survey, the world’s population of oculoplastic surgeons was initially stratified into 15 regions, with several regions corresponding to a national or international oculoplastic society. Each regional version of the survey (discussed above in Survey Design) was implemented in SurveyMonkey (https://www.surveymonkey.com) and participation was requested by email to oculoplastic society lists. Three such emails were sent requesting participation. Responses were collected during a 3-week period. Participation in the survey was anonymous, with responses grouped by region. As per the US Code of
Federal Regulations, this study falls outside the purview of institutional review board approval as it does not involve human participants. Participant (physician) consent was considered implicit with the voluntary response to the survey invitation.

Data Processing
On completion of the response collection period, a single worldwide data set was formed by merging the responses obtained from each region while creating a field for regional identity. Since language varied by region, responses were translated into a numerical representation that was equivalent for all regions, questions (other than location and free-text questions), and answer choices. All subsequent data processing and analysis was performed in Matlab (The Mathworks).

Statistical Analysis
Scripts were written in Matlab to compute response counts and response frequencies by practice location, training location, and survey region. These local summary measures were supplemented by the computation of worldwide summary measures. For questions with binary responses, worldwide means of positive response rates were calculated. For questions with categorical data and interval data, response modes were calculated. Standard sample size calculations were performed to determine polling accuracy.

To assess the factors influencing prescription of antibiotics in the postoperative period, regression analysis was performed using responses to the question regarding prescription of postoperative oral antibiotics as observations of a binary dependent variable. The independent variables considered were training location, practice location, time since training, fellowship type, academic vs private practice, urban vs rural practice, estimated wound infection rate without antibiotics, estimated allergic reaction rate with antibiotic use, and estimated gastrointestinal tract upset rate with antibiotic use. The nominal categorical variables practice location and training location were recoded as binary dummy variables to be included in the analysis. Ordinal and interval categorical variables were kept as categorical variables for the analysis. Regression analysis was performed by fitting a generalized linear model with binomial distribution and logit link function to the aforementioned predictor variables. A stepwise approach was used to remove noncontributory predictors from the model.26 All the aforementioned factors were specified prior to analysis. The association between antibiotic use and geographic latitude was assessed separately in a single post hoc analysis by computing the correlation coefficient between national prescribing rates and population-weighted latitude.

Map Generation
To rapidly assess global trends in question responses, results for each question were used to generate color-coded world maps. Scripts were written in Matlab to perform this operation in conjunction with the Matlab Mapping Toolbox. World vector maps at 1:50 scale with national borders were obtained from Natural Earth (http://www.naturalearthdata.com) and overlaid with survey data. Separate sets of maps were generated displaying data organized by practice location and training location.

Results

Respondent Characteristics
A total of 782 responses were obtained across all 15 societies to which the survey was distributed. The survey was distributed to a population of 2397 surgeons (average response rate 36.7%), resulting in a margin of error of 2.5% with 95% CIs. The nations or regions with the highest number of respondents by self-reported practice location were, in descending order, United States and Canada, United Kingdom, Spain, Brazil, and Argentina. Most respondents (56%) reported that it had been 11 or more years since they completed training, with 32.3% reporting that it had been between 11 and 20 years since they completed training. While respondents predominantly trained in academic settings (77.3%), a small majority of respondents currently work in private practice settings (53.1%). The vast majority of respondents currently practice in urban settings (93.5%) as opposed to rural areas.

Antibiotic Prescribing Rates
The survey included questions regarding the prescription of intravenous, oral, and topical antibiotics for routine, uncomplicated eyelid surgical procedures. A total of 13.5% of respondents reported giving patients perioperative intravenous antibiotics for routine, elective eyelid procedures. Postoperative oral antibiotics were prescribed more commonly, with 23.6% of respondents confirming their use for routine, uncomplicated eyelid surgical procedures. Topical antibiotics were far more commonly prescribed than either intravenous or oral antibiotics worldwide, with rates of 85.2% immediately after surgery and 87.9% for postoperative home care.

Wide variation was noted in postoperative oral antibiotic prescription rates by practice location, ranging from 2.9% in the United Kingdom to 86.7% in India among countries ranking in the top 10 for number of respondents. The variation in postoperative oral antibiotic prescription rates by practice location are depicted in the Figure. No similar wide variation was seen in the prescribing practices of intravenous or topical antibiotics.

Antibiotic-Related Factors
Factors related to antibiotic regimen were assessed with a set of 5 questions. Training (60.1%) and personal experience (58.1%) were the predominant reasons reported by respondents for their current antibiotic regimens. For those who changed their antibiotic regimens since training, personal experience (29.0%) and findings from the literature (16.5%) were the most commonly reported reasons for regimen changes. When asked to estimate the rate of unequivocal wound infection in routine, elective eyelid surgical procedures without the use of oral or intravenous antibiotics, the most common estimate (given by 34.6% of respondents) was 1%. When asked to estimate the rate of allergic reactions with the use of oral antibiotics, the majority of respondents (56.2%) estimated less
than 1%. Finally, when asked to estimate the rate of diarrhea induced by a 1-week course of oral antibiotics, 47.3% of respondents estimated between 2% and 10%. Distance from the equator was inversely correlated with oral antibiotic prescribing rate ($R = 0.50, P = .01$).

Regression Analysis
The results of the regression analysis are described in the Table. Regression analysis demonstrated that practicing in particular regions of the world had a statistically significant effect on the odds of prescribing oral antibiotics postoperatively. The practice locations that were the strongest predictors of routinely prescribing postoperative oral antibiotics were India (OR, 15.83; 95% CI, 4.85-51.68; $P < .001$), Venezuela (OR, 13.47; 95% CI, 1.43-127.19; $P = .02$), and Southeast Asia (OR, 2.80; 95% CI, 1.15-6.84; $P = .02$). Conversely, practice location in the United Kingdom (OR, 0.048; 95% CI, 0.0063-0.37; $P = .004$), Australia and New Zealand (OR, 0.15; 95% CI, 0.03-0.67; $P = .01$), and the United States and Canada (OR, 0.41; 95% CI, 0.23-0.72; $P = .002$) decreased the odds of postoperative oral antibiotic use in a statistically significant manner. Training in Argentina increased the odds of prescribing postoperative oral antibiotics (OR, 7.92; 95% CI, 2.80-22.39; $P < .001$). Distance from the equator was independently determined to correlate inversely with oral antibiotic prescribing rate ($R = -0.50; P = .01$).

In addition, estimated allergic reaction rate with antibiotic administration decreased the odds of prescribing oral antibiotics postoperatively (OR, 0.34; 95% CI, 0.23-0.49; $P < .001$), while estimated infection rates (without the use of oral antibiotics) increased the odds of prescribing oral antibiotics postoperatively (OR, 1.80; 95% CI, 1.45-2.23; $P < .001$).

Discussion
Given the limited alternatives available to mitigate multidrug resistance, physicians are compelled to justify the use of antibiotics with scientific evidence whenever possible. The only published review, to our knowledge, of prophylactic antibiotics following a subset of orbital surgery demonstrated the futility of that practice and highlighted some of the detriments associated with indiscriminate antibiotic prescription. The present survey was not designed to determine the efficacy of prophylactic antibiotic use but to document existing practices and to seek possible explanations for those practices in different geographic regions. Armed with the knowledge of their compatriots’ habits, eyelid surgeons should be better prepared to base their decisions on science alone.

Some individual eyelid surgeons lament the use of oral antibiotics for anticipated infections but continue to prescribe them because of perceived legal pressure or peer pressure and fear legal action or professional criticism were they to withhold oral antibiotics for a potentially avoidable infection. Others surgeons proclaim the importance of oral antibiotics with full confidence, despite evidence to the contrary. The current study was not designed to compare rates of infection or rates of untoward events with or without antibiotics. Instead, this survey documents practices and, given the paucity of data on which surgeons can base decisions, delves into the reasons for these disparate practices.

The intuition shared at the 2013 European Society of Ophthalmic Plastic and Reconstructive Surgery meeting did indeed prove true: prescribing rates for prophylactic oral anti-
biotics following uncomplicated eyelid surgery vary widely depending on geographic region. In our study, geographic location proved to be the single most important factor correlating with the likelihood of prescribing oral antibiotics. Among the 10 regions with the highest number of respondents, the United Kingdom had the lowest rate (2.9%), while India had the highest rate (86.7%). This difference persisted, albeit to a lesser degree, when comparing regions that are somewhat more similar and geographically closer. In Europe, the highest rate was found in Italy (41.7%), contrasting dramatically with the rate found in the United Kingdom (2.9%). In South America, Venezuela had the highest rate (83.3%), contrasting starkly with the rate in Chile (0%). Although great variation (22.5%) was seen in prescribing rates for oral postoperative antibiotics (the primary focus of this investigation), little variation was identified for intravenous or topical prophylaxis; the former is used to treat infection prophylaxis in preventive clinical trials involving patients undergoing plastic and reconstructive surgical procedures found no benefit to long- vs short-course antibiotic prophylaxis in preventing surgical site infections. Furthermore, the Centers for Disease Control and Prevention explicitly recommends that prophylactic antibiotics be administered only where a definite advantage has been demonstrated in the scientific literature: “Use an [antimicrobial prophylaxis] agent for all operations or classes of operations in which its use has been shown to reduce surgical site infection rates based on evidence from clinical trials or for those operations after which incisional or organ space surgical site infection would represent a catastrophe.”

The dangers of antibiotics to individuals and to communities are real. Resistance to antibiotics is increasing and multidrug-resistant bacteria (eg, methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, multidrug-resistant gram-negative bacilli) are now seen worldwide, primarily owing to selective pressure from widespread antibiotic use. Antibiotics in surgical prophylaxis contribute to that selective pressure, and the need for them must be carefully weighed. For the individual, the risk of an allergic reaction, including devastating reactions such as Stevens-Johnson syndrome or Clostridium difficile colitis, must be weighed against any potential benefit of having an antibiotic prescribed. Interestingly, the respondents to this survey underestimated these risks. For example, while most estimated a 2%-10% risk of antibiotic-associated diarrhea, the documented risk of diarrhea with a 1-week course of amoxicillin-clavulanate approaches 25%.

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### Table. Regression Analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Kingdom (practice)</td>
<td>0.048 (0.0063-0.37)</td>
<td>.004</td>
</tr>
<tr>
<td>Australia or New Zealand (practice)</td>
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<tr>
<td>Southeast Asia (practice)</td>
<td>2.80 (1.15-6.84)</td>
<td>.02</td>
</tr>
<tr>
<td>Argentina (training)</td>
<td>7.92 (2.80-22.39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Venezuela (practice)</td>
<td>13.47 (1.43-127.19)</td>
<td>.02</td>
</tr>
<tr>
<td>India (practice)</td>
<td>15.83 (4.85-51.68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Surgeons’ estimates of complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated rate of allergic reaction to antibiotics</td>
<td>0.34 (0.23-0.49)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Estimated rate of infection without oral antibiotics</td>
<td>1.80 (1.45-2.23)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

This survey was designed to investigate surgeon practices as one step in unveiling disparities in patterns of antibiotic use. A bias toward antibiotic use was seen in many fields of medicine from the 1970s through the 1990s, notably in otorhinolaryngology (sinusitis), pediatrics (airway infections), and surgery. The surgeons in this study acknowledged practice habits that date to their training or to the ambient culture but also confirmed a concern for legal liability and professional standards. Availability of antibiotics (eg, over-the-counter vs prescription, or owing to expense and insurance coverage) may also contribute to both patient expectations and physician practices. It is hoped this study (and the aforementioned retrospective orbital surgery study) will begin to provide support for evidence-based antibiotic decisions.

Currently, there is no consensus that would require the use of prophylactic oral antibiotics following eyelid surgery, while large-scale studies discourage any surgical prophylaxis beyond 24 hours postoperatively. Not only is there no evidence to support continuing antibiotics for surgical prophylaxis beyond 24 hours postoperatively for any type of surgery, but national guidelines advise against prolonged antibiotic prophylaxis. For plastic surgery procedures, there is also no evidence to support prolonged antibiotic prophylaxis. A recent meta-analysis of 12 randomized clinical trials involving patients undergoing plastic and reconstructive surgical procedures found no benefit to long- vs short-course antibiotic prophylaxis in preventing surgical site infections. Furthermore, the Centers for Disease Control and Prevention explicitly recommends that prophylactic antibiotics be administered only where a definite advantage has been demonstrated in the scientific literature: “Use an [antimicrobial prophylaxis] agent for all operations or classes of operations in which its use has been shown to reduce surgical site infection rates based on evidence from clinical trials or for those operations after which incisional or organ space surgical site infection would represent a catastrophe.”

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Diarrhea is only one obvious result of inadvertently manipulating the human microbiome (the collective genetic
material contained in the microbes that reside in and on humans). A link between antibiotics and childhood obesity was established as early as 1963, although research studies would not resume for several decades. Microbiota (trillions of intestinal bacteria) are now thought to be as specific to species and individuals as is native DNA, and disruption of that population can inhibit gastrointestinal tract absorption and allergen processing. Suppression of specific bacterial genes has been linked to disinhibition of T cells, with a subsequent rise in the prevalence of allergies and asthma. Additional effects undoubtedly remain to be discovered.

The current study has limitations, and it is important to limit the conclusions to the scope of the survey. For the purpose of uniformity, the survey included only eyelid surgeries who are members of oculoplastic societies and excluded others who may perform considerable eyelid surgery; some of those physicians may practice quite differently, even within the same geographic region, which represents a potential limitation of the study. It did not assess the risk of infection with or without antibiotic prophylaxis and did not compare the efficacy of topical, oral, or intravenous medications. Given the paucity of data documenting eyelid wound infections, the survey did not compare rates of infections between geographic regions. All these data and others would help develop more concrete guidelines for the use of antibiotics in oculoplastic surgery. Future work could include a randomized, prospective series, but it would be difficult to power given the rarity of infection. Additional work involves generating awareness among surgeons and patients, encouraging rational practice, and creating outcomes measures similar to those in other surgical specialties.

Conclusions

These survey results from members of ophthalmic plastic and reconstructive surgery societies suggest that antibiotic prescribing practices for routine eyelid surgical procedures vary widely throughout the world. These results could provide additional evidence for surgeons to consider when deciding on the benefits and risks of prophylactic antibiotics in an individual patient, especially considering the mounting evidence of the detrimental effects of such prescribing.

REFERENCES


