PERIOPERATIVE ANTIBIOTIC THERAPY IN OROFACIAL CLEFT SURGERY. WHAT IS THE CONSENSUS?

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ABSTRACT

Clefts of the primary and secondary palate represent one of the commonest congenital anomaly for which surgical correction is required. The perioperative care of the patients varies widely across centers and among surgeons and range from preoperative swab of palatal clefts for microbiological studies to prophylactic and or therapeutic antibiotic care. These practices have economic implications especially in the Low and Middle Income Countries (LMIC) where the cost of care are borne directly by the parents. The clinical implications of indiscriminate antibiotic use may also include development of resistant strains and hypersensitivity reactions which may be life threatening. Surgical site infections and its possible sequelae of dehiscence and fistulae is another concern for the surgeon and the patient.

This review examines the microbiological pathogens, surgeon's perspectives as well as the current evidences for the use of perioperative antibiotic therapy in orofacial cleft surgery and concludes with a need for a large multicenter randomized clinical trial to answer critical aspects of the subject.

Keywords: Cleft lip and palate, Orofacial clefts, Antibiotic in cleft surgery

INTRODUCTION

The oral cavity and nasopharynx of children with unrepaired cleft lip and palate are recognized to be at an increased risk of colonization by bacterial pathogens. Significant interest has been generated among clinicians about the role of infections in the development of complications following cleft surgery in these patients. A causal relationship has long been established between infection and failure of surgical repair[1-3].

Several publications on children with clefts have identified oral flora of microorganisms pre-operatively and the association of post-operative complications with pathogenic organisms found in the perioperative period[4-7]. These complications can result in systemic infection for the child, secondary heamorrhage, wound dehiscence, palatal fistulae with resultant prolonged hospital stay. Subsequent morbidities may include poor speech, impaired appearance and impaired facial development[8]. Hupkens *et al.*[9] reported a strong association between preoperative cultures especially of Group A Streptococcus and Staphylococcus aureus and postoperative palatal dehiscence. Previous studies have also confirmed that patients with orofacial clefts are at increased risk for the development of caries and periodontal diseases compared to noncleft children[10,11].

Primary closure of cleft lip and palate is classified as a clean contaminated operation, and wound infection is a recognized risk. The risks are associated with the duration of operation especially with primary cleft operations often requiring 1–2 h of operating time.[12] The consequences of surgical wound infection after repair of cleft lip or palate can be devastating in both the short and the long term. A major wound infection after primary repair of a cleft anomaly is likely to require a further admission for a secondary intervention; however, final outcomes such as speech and growth may also be compromised.

Antibiotics are likely to reduce the incidence of wound infection and complications, but this has never been clearly shown in randomized clinical trials in repair of clefts[8]. Despite the beneficial effects of antibiotics, its widespread use may result in increasing rates of antibiotic resistance in addition to increased cost of care especially for families making out of pocket payment for their children's care[13]. This can constitute additional burden on such parents. Unfortunately, there is currently no global, regional or national guidelines for the rational use of antibiotic prophylaxis in repair of orofacial clefts.

This review seeks to evaluate the arguments for or against the use of peri-operative antibiotics therapy for CLP surgeries based on available literature and draw conclusions that could guide rational choice by surgeons and other practitioners.

Bacteremia in Cleft and Oral Surgeries

Several studies have documented significant bacteremia following cleft lip and palate and intraoral surgeries[14-19]. These procedures were diverse and ranged from cleft lip and palate (CLP) surgeries, tooth extraction and removal of osteosynthesis plates, third molar surgeries and some maxillofacial procedures. Previous assertions have been that bacteremia associated with oral surgeries in healthy individuals is transient without significant sequel[20,21]. However, a recent study has documented bacteremia following cleft lip and palate surgeries persisting for up to 15 minutes in 53% of the patients[19]. The bacteremia in this group of patients was also higher than those for oral procedures such as orthodontic procedures and root scaling. The implication of the finding is that cleft-related surgery could be harmful in patients at risk, especially those with associated cardiac anomalies. Factors that were associated with development of bacteremia in patients with CLP anomaly included age less than 62.3 months and the male gender (59.4%), although these factors were not statistically significant. On the relationship between bacteremia and the specific type of surgery, the authors found that the prevalence of bacteremia in cleft lip surgery was 40.9%, whereas the incidence in cleft palate surgery was 33.3%. A prevalence of 50% was recorded for alveoloplasty. No reason was proposed for these differences. It was also found that bacteremia associated with CLP surgeries in the study was polymicrobial, similar to findings from several other studies that reported polymicrobial bacteraemia following other dental procedures[14,16,18,22]. These organisms in the oral cavity can gain access into the blood stream during these procedures[23-25].

Based on their findings, Adeyemo et al[19] advocated for the need for prophylactic antibiotic therapy for CLP because of the patients with associated congenital heart defects and the risks for bacteria endocarditis in this group of patients.

Bacteriology of Oral Flora

The oral cavity, which remains sterile throughout prenatal development, becomes a diverse ecosystem colonized by several microorganisms during the first few hours after delivery. The skin and mucus membranes of neonates are colonized by microbiota as a result of contact with the external environment. A significant part of the oral microbiota in the early neonatal period originates from the mother and is transient population of microorganisms consisting of intestinal bacteria[26]. The spectrum of organisms at this stage depends mainly on factors such as the gestational age of the baby, the mode of delivery, type of feeding and the length of hospital stay[26-32].

The early oral microbiota occurring within several hours following delivery is composed of viridans streptococci and Streptococcus salivarius (S. salivarius), which are commensals permanently colonizing the oral cavity[28]. Along with other bacteria, they participate in the formation of a "colonization cascade" that determines future indigenous microbiota[28,29,33]. Congenital orofacial malformation affects the structure and functions of the oral cavity, thereby significantly modifying its characteristics[9]. Both abnormal morphology and improper function of the oral cavity in newborns with cleft palate create a different environment from that of healthy neonates. Therefore, these abnormalities may affect oral microbiota[34].

The oral cavity is replete with diverse strains of microorganisms. Organisms that are commonly found include Staphylococcus aureus (SA) and b-hemolytic streptococci (bHS), when compared with the normal population[19,34,35]. More than 500 different bacteria strains have been identified in the oral cavity[36]. The oral microbial community is normally in equilibrium, but a compromise of the ecological balance can occur and result in surgical site infection. A list of the most important bacteria commonly isolated from the oral cavity is presented in Table 1[37].

Antibiotic Therapy in Cleft Surgery

Operations in the aero digestive tract are frequently considered as clean contaminated and the incidence of surgical site infections (SSI) is about 10 to 15% which represents a significant health burden[38]. By definition, a SSI is an infection that develops within 30 days after an operation or within 1 year of an implant being placed, where the infection appears to be related to the surgery[39]. Perioperative antibiotics are generally used in surgery to prevent SSI. In contrast to therapeutically used antibiotics, the perioperative treatment aims to reduce contamination of the bacterial flora in the specific surgical area. The basic purpose of antibiotic prophylaxis is, therefore, to provide an adequate drug level in the tissues before, during, and for the shortest possible time after the procedure[38]. Prophylactic antibiotic treatment is defined as the use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications. It has been estimated that approximately half of SSIs are preventable by application of evidence-based strategies[40].

Table 1: Bacteria commonly isolated from the oral cavity

Genus	Species
Strict anaerobic bacteria	
Gram-negative rods	
Porphyromonas	P. gingivalis, P. endodontalis, P. catoniae
Prevotella	P. oralis, P. oris, P. buccae, P. corporis, P. denticola, P. loescheii, P. intermedia, P. nigrescens, P. melaninogenica,
Fusobacterium	F. nucleatum spp. nucleatum, spp. vincentii, spp. polymorphum
Mitsuokella	M. dentalis
Selenomonas	S. sputigena, S. noxia
Campylobacter	C. sputorum, C. rectus, C. curvus
Treponema	T. denticola, T. vincentii, T. socranski
Bacteroides	B. forsythus
Gram-positive rods	
Eubacterium	E. alactolyticum, E. lentum, E. yurii
Propionibacterium	P. acnes, P. propionicus, P. jensenii, P. granulosum, P. avidum
Lactobacillus	L. catenaforme, L. crispatus, L. oris, L. uli, L. grasseri
Actinomyces	A. israelii, A. odontolyticus, A. meyeri
Arachnia	A. propionica
Gram-negative cocci	
Veillonella	V. parvula, V. alcalescens
Gram-positive cocci	
Peptostreptococcus	P. asaccharolyticus, P. magnus, P. micros, P. anaerobius P. prevotii
Facultative anaerobic bacteria	
Gram-negative rods	
Eikenella	E. corrodens
Capnocytophaga	C. ochracea, C. sputigena, C. gingivalis, C. haemolytica, C. granulosa
Actinobacillus	A. actinomycetemcomitans
Actinobacillus	A. actinomycetemcomitans
Haemophilus	H. aphrophilus H. influenzae, H. parainfluenzae, H. paraphrophilus, H. segnis
Gram-positive rods	
Corynebacteriu	C. xerosis, C. matruchotii
Actinomyces	A. naeslundii, A. viscosus
Rothia	R. dentocariosa
Lactobacillus	L. acidophilus, L. brevis, L. buchneri, L. casei, L. salivarius, L. fermentum
Gram-negative cocci	
Neisseria	N. flavescens, N. mucosa, N. sicca, N. subflava
Branhamella	B. catarrhalis
Gram-positive cocci	
Streptococcus	S. mutans, S. sanguis, S. salivarius, S. sobrinus, S. rattus, S. downei, S. mitis, S. milleri, S. oralis, S. intermedius, S. constellatus
Staphylococcus	S. aureus, S. epidermidis
Enterococcus	E. faecalis, E. faecium

Based on Mouton and Robert (2)

The Scottish Intercollegiate GL Network (SIGN) guideline "Antibiotic prophylaxis in surgery" defines two regimens; the short-term prophylaxis administered any time before or after surgery for up to 24 h after the surgical intervention and long-term antibiotic prophylaxis that is continued for longer than 24 h. In contrast, therapeutic antibiotic treatment is used to reduce the growth or reproduction of bacteria, including eradication therapy. Antimicrobial therapy is then prescribed to clear infection by an organism or to clear an organism that is colonizing a patient but is not causing infection[41].

Despite the obvious benefits of antibiotics, their excessive and indiscriminate use may not only be uneconomical but also result in the risk for developing multiple drug resistance in bacteria which is claimed to be a major cause of the failure of therapy in many human infections[42]. Therefore, appropriate use of antibiotics is seen as a national health priority to prevent the morbidity of infections and the development of resistant organisms[40].

The consequences of surgical wound infection after repair of cleft lip or palate can be devastating in both the short and the long term. A major wound infection after primary repair of a cleft is likely to require a further admission for a secondary intervention; however, final outcomes such as speech and growth may also be compromised. Antibiotics are likely to reduce the incidence of wound infection and complications[8] but there are limited randomized clinical trials on the use of perioperative antibiotics in repair of clefts.

A survey among surgeons doing primary cleft surgery in the UK and Ireland showed a lack of consensus and considerable disparity among cleft centres in the UK about antibiotic prophylaxis for primary cleft surgery. Most of these cleft surgeons use an antibiotic for prophylaxis during repair of a cleft lip, some surgeons continue this for 5 days although there is no supporting evidence of additional benefit. Unusually, a slightly higher proportion of surgeons would not use any form of antibiotic prophylaxis for repair of a cleft palate than for isolated repair of a cleft lip, and although nearly half would not use any antibiotic prophylaxis afterwards, a third would continue to give it for 5 days[8].

A similar survey among members of the American Cleft Palate-Craniofacial Association found out that eighty-five percent of the surgeons administered prophylactic antibiotics, including 26% who used a single preoperative dose. A further 23% gave 24 hours of postoperative therapy; 12% used 25 to 72 hours, 16% used 4 to 5 days, and 12% used 6 to 10 days. Five percent of surgeons administered penicillin, 64% administered a first-generation cephalosporin, 13% administered ampicillin/sulbactam, and 8% gave clindamycin. The authors also retrospectively reviewed 311 patients out of which 173 received antibiotics and 138 did not. They found out that delayed healing and fistula rates did not differ between the groups: 16.8% versus 15.2% ($p = 0.71$) and 2.9% versus 1.4% ($p = 0.47$), respectively[43].

A prospective, double blind randomized placebo controlled clinical trial conducted in India reported a higher incidence of early complications (13.8%) among the patients in the placebo group compared to 8.7% ($p=0.175$) in the antibiotic group which consisted of a five-day course of postoperative oral amoxicillin (50mg/kg/day). The study also found a higher incidence of fistulae (17.1%) in the placebo group compared to the antibiotic group (10.7%) ($p= 0.085$). These differences in the early and late complication rates were however not statistically significant[44]. A large retrospective series comprising 3,108 patients from India found no difference in the wound infection rates between the group which had postoperative antibiotics and the group which did not[45].

CONCLUSION

Although the efficacy of perioperative prophylactic antibiotics in preventing postoperative wound infections after clean-contaminated surgery where the aerodigestive tract is violated has been clearly established in clinical trials[46-48], only scarce evidence exists for its use in cleft lip, alveolus and palate surgery. Primary efficiency endpoint was occurrence of postoperative fistulae. Here, antibiotic prophylaxis as single shot or 5-day regime failed to show reduction of statistical significance[43,44]. In addition, incidence of wound infections was low even without the use of postoperative antibiotics[45]. Up to date, the use of antibiotic prophylaxis in cleft lip and palate surgeries have not been substantiated. A large multicenter randomized clinical trial with specific selection criteria is recommended to further elucidate the benefit or otherwise of prophylactic and therapeutic antibiotic therapy in the surgical management of orofacial cleft.

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