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ANTIBIOTIC ADMINISTRATION IN FACIAL AND SKULL FRACTURES
Evidence Based Medicine Guideline

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SUMMARY
Antibiotic administration in patients with facial and skull fractures can be divided into four phases: non-operative, preoperative (time of admission until operation), perioperative (prior to incision but not greater 24 hours postoperatively) and postoperative (greater than 24 hours following the operation). Antibiotic administration is supported by the literature for the *perioperative* phase, but not the non-operative, preoperative, or postoperative phases with the possible exception of mandibular fractures.

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **Perioperative antibiotics significantly decrease postoperative infections in facial fractures**
  - **If prophylactic antibiotics are utilized, use short course therapy (<24 hours)**
- **Level 3**
  - **Antibiotic administration is not recommended in patients with non-operative facial fractures as it does not decrease the rate of infection**
  - **For non-operative sinus fractures, utilize empiric coverage with amoxicillin/clavulanic acid or ampicillin/sulbactam for 3-5 days due to high risk of infection**
  - **Prophylactic antibiotics**
    - **Open mandibular fractures: ampicillin/sulbactam 3 gm IV q 6hr for 24 hrs post-operatively**
    - **All other operative facial fractures: cefazolin 1 g IV q 8hr for 24 hrs post-operatively**
  - **For closed and/or basilar skull fractures with or without cerebrospinal fluid (CSF) leak, do not use prophylactic antibiotics**
  - **For open skull fractures without contamination: cefazolin 2 g IV q 8hr for 3 days**
  - **For open skull fractures with significant contamination: ceftriaxone 2 g IV q 12hr +/- metronidazole 500 mg IV q 8hr for 3 days**
  - **Pneumococcal vaccination should be given in patients with basilar skull fractures and CSF leak**
    - **13-valent pneumococcal conjugate vaccine (Prevnar13) administered during hospitalization followed by 23-valent pneumococcal polysaccharide vaccine (Pneumovax) at least 8 weeks after the Prevnar13 dose**
  - **Hydrogen peroxide should be avoided as an irrigant or daily wound care**
  - **Triple antibiotic ointment applied three times per day for one week until follow up may be beneficial for sutured lacerations to reduce infection rate**

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

INTRODUCTION

Facial fractures are a common diagnosis in the United States with approximately 3 million individuals sustaining craniofacial trauma on an annual basis. Many of these patients received antibiotics as part of their care (1). The prevention of surgical site infections (SSI) has become a primary focus of hospitals across the nation as a metric of quality care. Antibiotic stewardship has become a primary focus, in part due to the increasing awareness of drug-resistant organisms as well as increased reporting of drug side effects.

A survey of experts reported use of preoperative antibiotics in 47-69% of patients, perioperative antibiotics in 94-100% of patients, and postoperative antibiotics in 65-71% of patients depending on facial fracture type (2). The use of antibiotics in this manner is not supported by the available literature regarding appropriate use of antibiotics in facial fractures.

Skull fractures can be divided into 3 categories: linear fractures, depressed fractures, and basilar fractures. Basilar skull fractures are the most common type of skull fracture to require intervention. The estimated incidence of basilar skull fractures (BSF) from non-penetrating head trauma is 7-16% (3). Concurrent cerebral spinal fluid (CSF) leakage occurs in approximately 10-30% of skull base fractures and can be associated with a higher risk of meningitis. The use of prophylactic antibiotics in this patient population is traditionally thought to prevent posttraumatic meningitis, which occurs at a rate of 1-20%. However, there has not been consistent evidence to support this hypothesis.

Further studies are needed to define the role of antibiotics on a granular level for both skull and facial fractures with specific attention to known risk factors for infection, fracture complexity and specific antibiotic regimens.

LITERATURE REVIEW

Facial Fractures

Nonoperative Antibiotic Administration

Malekpour et al. retrospectively compared the administration and duration of antibiotic prophylaxis on the incidence of soft tissue infection in non-operative facial fractures (4). Patients were categorized into 3 groups: no antibiotic prophylaxis, short-term antibiotic prophylaxis of 1-5 days, and long-term antibiotic prophylaxis of >5 days. Ampicillin/sulbactam, amoxicillin/clavulanic acid, or clindamycin were administered to those in the antibiotic prophylaxis groups. Baseline facial fractures were statistically different between groups. Patients who did not receive antibiotics more commonly had a single facial fracture (80%). Those that received short-term antibiotics and long-term antibiotics more commonly had both maxillary and orbital fractures (54% and 60% respectively). No patient in the study developed soft tissue infection.

Zosa et al. (discussed in detail below) performed a subgroup analysis of patients with facial fractures managed non-operatively with the most common fracture type being midface fractures (5). A total of 293 patients were identified that had received non-operative management. Fifty-nine patients (20%) received an extended antibiotic course (>24 hours) compared to 234 patients (80%) that received short-course antibiotics (<24 hours). There was no significant difference in rate of head or neck infections between groups (3.4% vs 5.2%; p=0.46).

Schmidt et al. randomized 50 patients who presented after blunt traumatic maxillary sinus fractures to receive saline spray plus 3 days of antibiotics or saline spray alone (6). The most common fracture patterns included zygomaticomaxillary complex fractures (36%) and isolated orbital floor fractures (30%). The primary outcome of acute sinusitis was assessed after a minimum of 3 days. The clinical rate of acute sinusitis after maxillary sinus fracture was high (95% in antibiotic group vs. 88% in saline group). While these rates were high, a 3-day course of antibiotics did not prevent infection.

Forrester et al. performed a systematic literature review for the Surgical Infection Society (SIS) Guidelines for Antibiotic Use in Patients with Traumatic Facial Fractures (7). This group identified 3 trials for the subgroup of nonoperative midface, upper face, or mandibular facial fractures. The SIS concluded that there is no clear benefit to antibiotic administration in patients with nonoperative midface, upper face, or mandibular facial fractures after trauma.

Preoperative Antibiotic Administration

Zosa et al. retrospectively studied the outcomes of patients presenting to a Level 1 trauma center intensive care unit with isolated injuries to the head & neck with at least 1 facial fracture (5). Two groups receiving initial

prophylactic antibiotics received either a short course (<24 hours) (n=280) of antibiotics or an extended course (>24 hours) (n=123). Subsequent head and neck infection rates were compared for the two groups. Propensity score-matched analysis found no differences in head & neck infection rates between the two groups. In combined group analysis, independent risk factors for developing head & neck infections included younger age, penetrating injury type, open fractures, upper face or mandibular fractures, multiple fractures, vascular injury and hypertension.

Mamthashri et al. prospectively studied 50 patients undergoing open reduction and internal fixation for compound facial fractures (8). Patients were assigned to two study arms, the first receiving antibiotics at the time of admission and the second receiving antibiotics upon induction of anesthesia. The two groups were evaluated for endpoints of pain scores and perceived infection as determined by local erythema, swelling, fever and purulent discharge. No statistical difference in outcome was noted.

Linkugel et al. retrospectively studied 269 patients who were treated for mandible fractures and evaluated outcomes of infection as well as hardware complications (9). Patients who received both preoperative and perioperative antibiotics (n=216) were compared against patients receiving only perioperative antibiotics (n=53). No statistical difference in outcome was present.

Kyzas et al. in a systematic review of literature identified that there was a paucity of high-powered, descriptive randomized controlled trials evaluating the use of prophylactic antibiotics in compound mandibular fractures (1). Among 31 eligible studies, there was agreement that prophylactic antibiotics were superior to no antibiotics in preventing infection though the degree to which this was true, and number needed to treat, could not be determined.

Perioperative Antibiotic Administration

Chole et al. performed a randomized control trial comparing infection rates in patients with facial fractures who had not received pre-operative prophylactic antibiotics (10). 101 patients were randomized into two groups, one which received no perioperative antibiotics and another which received cefazolin 1 gm IV one hour prior to the surgical procedure and a second dose eight hours later. Of these patients, 79 had mandibular fractures, 18 zygoma fractures, and four Le Fort fractures. The group receiving antibiotics had a statistically significant decrease in postoperative infections compared to the no-antibiotic group (9% vs 42%).

Postoperative Antibiotic Administration

Baliga et al. prospectively studied 60 patients undergoing open reduction and internal fixation of zygomatic and mandibular fractures who received preoperative and intraoperative antibiotic dosing (11). Patients were divided into two arms; the first 30 received additional postoperative antibiotics and the second 30 did not. These patients were evaluated for evidence of infection at 7- and 21-days post operatively. There was no statistical difference in outcome between the two groups.

Soong et al., in a randomized, double-blind, placebo-controlled study, evaluated the rate of postoperative wound infections in patients with displaced Le Forte or zygomatic fractures that required operation (12). All patients received amoxicillin/clavulanic acid 1.2 g IV q 8 hours from the time of admission until 24 hours postoperatively. The first group received placebo only and the second group continued to receive amoxicillin/clavulanic acid 625 mg PO q 8 hours for 4 additional days. These patients were evaluated at 1, 2, 4, 6, and 12 weeks for evidence of infection and wound breakdown. There were no significant differences in the incidence of infection or side effects between the two groups. Schaller et al., in an identical study, evaluated the rate of postoperative wound infections in patients with mandibular fractures requiring operation (13). Again, no significant differences in infection rate were found. Zix et al., from the same group of investigators, performed an identical study in orbital blow-out fractures requiring operation (14). No significant difference found in infection rates between the two groups.

Mottini et al. performed a retrospective study to evaluate the influence of postoperative antibiotic duration on the rate of wound infections for patients presenting with uncomplicated mandibular and midfacial fractures (15). Patients were divided into two groups: group A (n=125) received 1 day of postoperative antibiotics, and group B (n=214) received 5 or more days of postoperative antibiotics. The antibiotic used for both groups was amoxicillin/clavulanic acid 1.2 g IV q 8 hours. Within the follow-up period of 6 months, 5 patients from group A (4%) and 7 patients from group B (3.3%) developed infections, resulting in no significant difference.

Habib et al. in a systematic review and meta-analysis of 13 studies identified that routine use of postoperative antibiotic prophylaxis with maxillofacial fractures is not necessary (16). The addition of postoperative antibiotic

prophylaxis to a standard preoperative and/or perioperative antibiotic regimen showed no significant difference in the risk of surgical site infection.

Campos et al. evaluated the efficacy of postoperative antibiotic prophylaxis for facial fractures in a prospective, randomized, controlled trial (17). Prior to surgery, both groups received a single dose of 2 g of cefazolin. Group I (n=42) did not receive additional antibiotics postoperatively. Group II (n=32) received cefazolin 1 g for 24 hours postoperatively. Within the 6-week follow-up, 7 patients from group I and 1 patient from group II presented postoperative infections resulting in no significant difference. Differences were detected when identifying mandibular fractures alone, with group II proving to be more efficacious than group I.

Wound Management in Open Fractures

In patients with open facial wounds, thorough irrigation should be performed. Studies have evaluated the effectiveness of various irrigants on infection rates comparing tap water, normal saline, and 1% povidone-iodine solution. These studies have shown no statistically significant benefit to any irrigant (18-20).

The use of hydrogen peroxide as an irrigant has become less favored after several studies demonstrated negative effects on wound healing (21-24). One study noted an inhibitory effect on keratinocyte migration, decreasing proliferative potential of cells (23). A more recent study analyzed the effects of hydrogen peroxide on various sutures noting a significant decrease in tensile strength of fast-absorbing gut sutures which are commonly used in head and neck repairs (24). While this study was performed in the lab, they hypothesized that hydrogen peroxide irrigants could lead to early breakdown of suture and increased risk for hypertrophic scarring.

Studies regarding the use of antibiotic irrigation for facial fracture wounds are lacking. Studies evaluating the use of topical antibiotics, however, suggest possible benefit (21,25). One randomized control trial studied a three times per day application of four different ointments on wound infection rates (25). All three antibiotic regimens were statistically superior to petrolatum alone in reducing the incidence of wound infection rates as follows:

- Petrolatum (control group): 17.6%
- Bacitracin zinc ointment: 5.5%
- Bacitracin zinc, neomycin sulfate, and polymxin B sulfate combination ointment: 4.5%
- Silver sulfadiazine cream: 12.1%

Skull Fractures

The 2017 Infectious Disease Society of America's (IDSA) clinical practice guidelines for healthcare associated ventriculitis and meningitis make the following recommendations regarding the use of prophylactic antibiotics (26):

1. Preoperative antibiotic prophylaxis is recommended for all patients *(strong, high)*
2. Antibiotic prophylaxis is not recommended for basilar skull fractures with CSF leak *(strong, moderate)*
3. CSF leak >7 days – consider surgical repair *(strong, low)*
4. Pneumococcal vaccination is recommended for patients with basilar skull fracture and CSF leak *(strong, moderate)*

Open, Penetrating Skull Fractures

Demetriades et al. conducted a randomized, controlled trial assessing evidence of intracranial or extracranial infection in patients presenting with an open skull fracture or a basilar skull fracture (27). Patients were excluded if surgical intervention was required. A total of 37 patients were split into three groups: group A with no antibiotics (n=12), group B with ceftriaxone 1 g IV daily for 3 days (n=14), and group C with ampicillin/sulphadiazine 1 g/ 0.5 g IV every 6 hours for 3 days (n=11). The incidence of meningitis occurred once (8.3%) in the group with no antibiotics and did not occur in either group that received antibiotics.

A systematic review from January 1966 to January 2000 identified 14 articles that studied antibiotic prophylaxis in patients diagnosed with penetrating brain injuries (28). The included articles were divided by patient population: military vs civilian. Both groups received broad spectrum antibiotics. It was found that the incidence of intracranial infection was lower (1-5%) in civilian patients compared to military patients (4-11%), likely due to the level of contamination. Infectious complications were also more frequent when CSF leaks, air sinus wounds, transventricular injuries, or those that cross the midline occurred.

Basilar Skull Fractures with or without CSF Leak

Friedman et al. retrospectively reviewed patient charts in whom traumatic CSF leaks secondary to basilar skull fracture had been diagnosed (29). A total of 43 patients were identified; 29 patients were treated with antibiotics and 14 patients were not. The specific antibiotics used by each patient were not disclosed. Twenty-four of the 43 patients were treated surgically. Three (10%) of the patients treated with antibiotic prophylaxis developed meningitis as did 3 (21%) of the patients who did not receive prophylaxis. Even though the difference was not statistically significant (p=0.33), the percent difference is large (11%).

Baltas et al. retrospectively studied the incidence of posttraumatic meningitis (30). A total of 860 patients were identified to have moderate to severe head injuries and had received some variation of antibiotic prophylaxis. Twelve patients out of 860 (1.4%) developed meningitis with 9 of those patients having basilar skull fractures and 7 having CSF leakage. The authors' conclusion is that meningitis is a rare complication of head trauma but does develop more commonly in patients with basilar skull fractures or CSF leakage.

Villalobos et al. performed a meta-analysis reviewing antibiotic prophylaxis for basilar skull fractures with and without CSF leakage (31). Twelve studies met inclusion criteria resulting in a total of 1,241 patients, with 719 (58%) patients receiving antibiotics and 522 (42%) not. Among those that received antibiotics, different antibiotic regimens were utilized including penicillins, first-generation and second-generation cephalosporins, and sulfonamides. Antibiotics were variably continued for 3 days to at least 1 week after CSF leakage. Overall results suggest that antibiotic prophylaxis did not prevent meningitis in those that received antibiotics vs. those that did not (OR 1.15; 95% CI 0.68-1.94; p=0.68). A subgroup analysis was performed in patients with CSF leakage (547 patients). 297 patients received antibiotics and 250 patients did not. Of those that received antibiotics, 29 (9.8%) developed meningitis, and of those that did not receive antibiotics, 34 (13.6%) developed meningitis. This difference was not statistically significant (p=0.28).

Eftekhar et al. prospectively studied the efficacy of prophylactic ceftriaxone 1 g twice daily for 5 days for the prevention of meningitis in patients with acute traumatic pneumocephalus (32). A total of 109 patients were identified and were divided into two groups – those that received prophylactic ceftriaxone (n=53) and those that did not (n=56). The overall rate of meningitis was 20%, with meningitis occurring in 19% in the antibiotic group and 21% in the control group (p=not significant). The results were the same when adjusted for variables such as presence of CSF leak, skull base fractures, and age.

Hoff et al. in a randomized controlled trial enrolled 160 participants that had a diagnosis of a basilar skull fracture without CSF leakage (33). The trial blindly assigned participants to one of three groups: no antibiotic, 1.2 million units of penicillin IV daily for three days, or 20 million units of penicillin IV daily for three days. No cases of meningitis occurred.

Ratilal et al. performed a systematic review in patients with basilar skull fractures to determine if antibiotic prophylaxis prevented meningitis (3). Five randomized controlled trials (n=208) were identified to meet inclusion criteria of comparing any antibiotic vs. placebo or no intervention for preventing meningitis. When evaluating the five included trials, there was no significant differences between antibiotic prophylaxis and control groups in terms of preventing meningitis [OR 0.69 (0.29-1.61)]. All-cause mortality, meningitis-related mortality, and need for surgical correction in patients with CSF leakage were also not found to have significant differences between groups. Most of the data in this systematic review (73%) originates from Eftekhar et al. (31) and Hoff et al. (32).

REFERENCES

1. Kyzas PA. Use of antibiotics in the treatment of mandible fractures: a systematic review. J Oral Maxillofac Surg 2011; 69(4):1129-1145.
2. Mundinger G, Borsuk D, Okhah Z, Christy M, Bojuvic B, Dorafshar A, Rodriguez E. Antibiotic and Facial Fractures: Evidence-Based Recommendations Compared with Experience-Based Practice. Craniomaxillofac Trauma Reconstr 2015; 8(1):64-78.
3. Ratilal BO, Costa J, Pappamikail L, Sampaio C. Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures. Cochrane Database of Syst Rev 2015; (4):CD004884.
4. Malekpour M, Bridgham K, Neuhaus N, et al. Utility of prophylactic antibiotics in nonoperative facial fractures. J Craniofac Surg 2016; 27(7):1677-1680.
5. Zosa BM, Elliott CW, Kurlander DE, Johnson F, Ho VP, Claridge JA. Facing the facts on prophylactic antibiotics for facial fractures: 1 day or less. J Trauma Acute Care Surg 2018; 85(3):444-450.
6. Schmidt RS, Dodson KM, Goldman RA. Prophylactic antibiotic therapy for fractures of the maxillary sinus. Ear Nose Throat J 2015; 94(4-5):170-177.
7. Forrester JD, Wolff CJ, Choi J, Colling KP, Huston JM. Surgical Infection Society guidelines for antibiotic use in patients with traumatic facial fractures. Surgical Infections. 26 Jun 2020. Ahead of print http//doi.org/10.1089/sur.2020.107.
8. Mamthashri V, Reddy BP. Comparison of Preoperative and Perioperative Antibiotic Prophylaxis Regimen in Compound Facial Fractures. J Contemp Dent Pract 2018; 19(2):214-220.
9. Linkugel AD, Odom EB, Bavolek RA, Snyder-Warwick AK, Patel KB. Systemic Preoperative Antibiotics with Mandible Fractures: Are They Indicated at the Time of Injury? Craniomaxillofac Trauma Reconstr 2018; 11(1):35-40.
10. Chole RA, Yee J. Antibiotic prophylaxis for facial fractures. A prospective, randomized clinical trial. Arch Otalaryngol Head Neck Surg 1987; 113(10):1055-1057.
11. Baliga SD, Bose A, Jain S The evaluation of efficacy of post-operative antibiotics in the open reduction of the zygomatic and mandibular fracture: a prospective trial. J Maxillofac Oral Surg 2014; 13(2):165–175.
12. Soong PL, Schaller B, Zix J, Lizuka T, Mottini M, Liegger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 3: Le Fort and zygomatic fractures in 94 patients. Br J Oral Maxillofac Surg 2014; 52(4):329-333.
13. Schaller B, Soong PL, Zix J, Lizuka T, Liegger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 2: Mandibular fractures in 59 patients. Br J Oral Maxillofac Surg 2013; 51(8):803-807.
14. Zix J, Schaller B, Lizuka T, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 1: orbital fractures in 62 patients. Br J Oral Maxillofac Surg 2013; 51(4):332-336.
15. Mottini M, Wolf R, Soong PL, Lieger O, Nakahara K, Schaller B. The role of postoperative antibiotics in facial fractures: comparing the efficacy of a 1-day versus a prolonged regimen. J Trauma Acute Care Surg 2014; 76(3):720-724.
16. Habib AM, Wong AD, Schreiner GC, Satti KF, Riblet NB, Johnson HA, Ossoff JP. Postoperative prophylactic antibiotics for facial fractures: a systematic review and meta-analysis. Laryngoscope 2019; 129(1):82-95.
17. Campos GBP, Lucena EES, da Silva JSP, Gomes PP, Germano AR. Efficacy assessment of two antibiotic prophylaxis regimens in oral and maxillofacial trauma surgery: preliminary results. Int J Clin Exp Med 2015; 8(2):2846-2852
18. Fernandez R, Griffiths R. Water for wound cleansing. Cochrane Database Syst Rev 2012;(2):CD003861
19. Dire DJ, Welsh AP. A comparison of wound irrigation solutions used in the emergency department. Ann Emerg Med 1990; 19(6):704–708.
20. Ghafouri HB, Zavareh M, Jalili F, Cheraghi S. Is 1% povidone-iodine solution superior to normal saline for simple traumatic wound irrigation? Wound Med 2016; 15:1–5.
21. Medel N, Panchal N, Ellis E. Postoperative care of the facial laceration. Craniomaxillofacial trauma & reconstruction 2010; *3*(4):189–200.
22. Brown C DZJ. Choice of Wound Dressings and Ointments. Shelton, CT: BC Decker; 2009.
23. O'Toole EA, Goel M, Woodley DT. Hydrogen peroxide inhibits human keratinocyte migration. Dermatol Surg 1996; 22:525–529.
24. Athre S, Park J, Leach JL. The effect of a hydrogen peroxide wound care regimen on tensile strength of suture. Arch Facial Plast Surg 2007; 9:281–284.
25. Dire DJ, Coppola M, Dwyer DA, Lorette JJ, Karr JL. Prospective evaluation of topical antibiotics for preventing infections in uncomplicated soft-tissue wounds repaired in the ED. Acad Emerg Med 1995; 2:4–10.

26. Tunkel AR, Hasbun R, Bhimraj A, et al. 2017 Infectious Diseases Society of America's clinical practice guidelines for healthcare-asscoiated ventriculitis and meningitis.
27. Demetriades D, Charalambides D, Lakhoo M, Pantanowitz D. Role of prophylactic antibiotics in open and basilar fractures of the skull: a randomized study. Injury 1992; 23(6):377-380.
28. Anonymous. Antibiotic prophylaxis for penetrating brain injury. J Trauma 2001; 51:S34–40.
29. Friedman, JA, Ebersold MJ, Quast LM. Persistent posttraumatic cerebrospinal fluid leakage. Neurosurg Focus 2000; 9(1):1-5.
30. Baltas I, Tsoulfa S, Sakellariou P, et al. Posttraumatic meningitis: bacteriology, hydrocephalus, and outcome. Neurosurgery 1994; 35(3):422-426.
31. Villalobos T, Arango C, Kubilis P, Rathore M. Antibiotic prophylaxis after basilar skull fractures: a meta-analysis. Clin Infect Dis 1998; 27(2):364-369.
32. Eftekhar B, Ghodsi M, Nejat F, et al. Prophylactic administration of ceftriaxone for the prevention of meningitis after traumatic pneumocephalus: results of a clinical trial. J Neurosurg 2004; 101(5):757-761.
33. Hoff JT, Brewin A, U HS. Letter: antibiotics for basilar skull fracture. J Neurosurg 1976; 44(5):649.