Antibiotic use in mandibular fracture surgery – An international survey and a review of the literature Marko Oksa^{1, 2}, Aleksi Haapanen^{1, 2}, Frida Stråhlman¹, Johanna Snäll^{1, 2}

SUMMARY

Objective. To clarify antibiotic use by oral and maxillofacial surgeons in mandibular fracture patients and evaluate practices based on scientific evidence.

Material and methods. We assessed antibiotic use in simple symphysis and angle mandibular fractures among oral and maxillofacial surgeons in the Nordic countries through an e-survey. In addition, we performed a literature review of antibiotic administration in mandibular fracture surgery.

Results. A total of 41 oral and maxillofacial surgeons who treat mandibular fractures responded to the questionnaire. Timing and duration of antibiotic use varied. The duration of postoperative antibiotic treatment ranged from 1 to 7 days (mean 5.6 days). Respondents' practices were not in concordance with scientific evidence. According to previous studies, restricting antibiotic exposure to a maximum of 24 hours postoperatively was not related to a higher risk of surgical site infections. No articles described a benefit of prolonged postoperative antibiotic therapy.

Conclusions. Antibiotic use in connection with mandibular fracture treatment varied in the Nordic countries and antibiotic practices are not in concordance with the current literature. Restricting antibiotic exposure to a maximum of 24 hours postoperatively should be considered. Clear guidelines for antibiotic prophylaxis as part of the surgical management of mandibular fractures are required.

Keywords: mandible, fracture, antibiotics, prophylaxis.

INTRODUCTION

According to a multicenter and prospective study from 2012 covering European populations, mandibular fractures are the most frequent fractures in the maxillofacial area (1). Due to a possible risk of contamination with the oral flora, fractures in the dentate part of the mandible are prone to infections. Thus, prescribing prophylactic antibiotics as part of the treatment of mandible fractures seems to be compulsory (2).

Previous studies (3, 4) have shown that there is no evidence to support prolonged antibiotic prophylaxis in addition to perioperative antibiotic therapy as part of the surgical treatment of mandibular fractures. In 2006, Andreasen et al. (5) published a systematic review of prophylactic administration of antibiotics in the treatment of maxillofacial fractures. They concluded that in the treatment of

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mandibular fractures, excluding the condylar part of the mandible, a single-dose or 1-day prophylactic antibiotic therapy is the method of choice in reducing infections. Additionally, some studies (6-8) revealed that postoperative administration of antibiotics does not have a statistically significant benefit compared to only preoperative or perioperative antibiotic therapy (or both) in reducing surgical site infection (SSI) rates.

The use of perioperative antibiotics as part of the surgical treatment of mandibular fractures is well established, but there are no data to support prolonged postoperative administration of antibiotics (6). The absence of protocols and antibiotic guidelines may lead to wide variation in antibiotic use practices. A reduction in antibiotic use will limit the development of antimicrobial resistance, which is a severe problem throughout the world (9).

The aim of the present study was to assess the use of antibiotics by oral and maxillofacial surgeons in mandibular fracture patients in the Nordic countries. We hypothesized that treatment practices may vary, and evidence-based treatment recommendations are required. We conducted a literature

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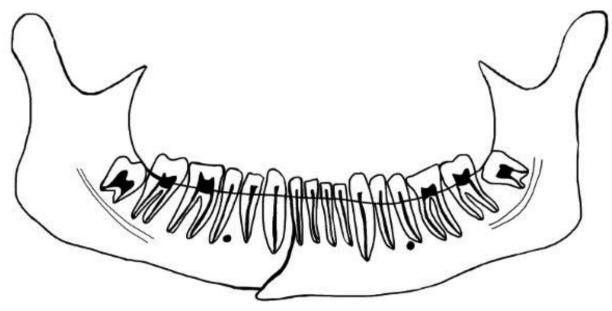


Fig 1. A patient with a fracture in the symphysis region

review on current research to compare our findings to existing practices.

MATERIALS AND METHODS

Study design

The study was conducted in two parts.

In the first part, we assessed antibiotic use practice by oral and maxillofacial surgeons. The e-survey was designed and conducted between 5 April 2019 and 28 February 2020. The second part focused on previous research evidence and consisted of a literature search.

Survey

The e-survey was directed at oral and maxillofacial surgeons currently working in the Nordic countries. The Danish, Estonian, Finnish, Icelandic, Norwegian and Swedish oral and maxillofacial surgery foundations were contacted by email and asked to distribute an English-language questionnaire to their members. The survey was targeted at specialists treating mandibular fractures in their daily work. Trainees were excluded from the analyses.

Background information of respondents was collected at the beginning of the survey. Differences in the use of antibiotics in conjunction with intraoral surgical treatment of mandibular fractures were based on the following two fictitious patient cases: 1) a patient with a recent fracture of the mandibular symphysis (Figure 1) and 2) a patient with a recent fracture in the angulus region and a partially erupted third molar in line with the fracture (Figure 2). The fictitious patients did not have history of chronic disease and did not smoke or drink alcohol. They were described to be cooperative and had moderate pain.

The questions concerned the primary choice of antibiotic at different stages of treatment and the duration of postoperative antibiotic treatment. We also asked about the timeframe to operate on a similar fracture. The responses were collected using Google Forms.

Literature review Search strategy

Pubmed was searched to identify articles published before April 2020 using the following search terms: "mandibular", "fracture", "trauma", "mandible fracture", "antibiotics" and "prophylaxis". This query retrieved 134 publications. The complete form of the search query is presented in Appendix.

Study selection

Titles and abstracts of the retrieved publications were screened to exclude studies that did not focus on antibiotic prophylaxis as part of the surgical treatment of mandibular fractures, publications not written in English, and studies involving animal models. No duplicates were identified. To be included in this literature review, studies had to focus on antibiotic timing or length, and the relation between the antibiotic regimen and postoperative infection had to be clearly defined. Furthermore, only clinical studies were included in this review.

RESULTS

Survey

A total of 45 Estonian, Finnish, Icelandic, Norwegian, and Swedish oral and maxillofacial surgeons responded to the questionnaire, three of which

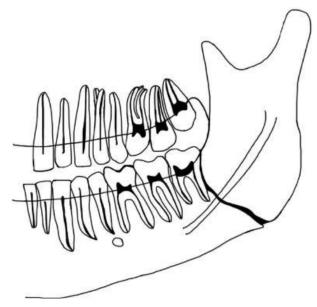


Fig 2. A patient with a fracture in the angulus region

were excluded because they were not specialists. One respondent who was not treating mandibular

Degree	n	%
MD	1	2.4
DDS/DMD	28	68.3
Both MD and DDS/DMD	12	29.3
Age	Range	Mean
	31–62	48.2
Sex	n	%
Women	10	24.4
Men	31	75.6

Table 1. Background information

fractures was excluded from the analyses. Thus, 41 respondents were included in the analyses. Background information is presented in Table 1.

In the case of symphysis fractures, 39 of 41 respondents (95.1%) reported antibiotic use as part of treatment. Thirty-six respondents (92.3%) favored antibiotic use immediately after fracture diagnosis. All respondents who reported prescribing antibiotics as part of the surgical treatment of mandibular symphysis fractures prescribed antibiotics in conjunction with surgery. Most of the respondents (34 of 39, 87.2%) reported using antibiotics postoperatively. The median reported duration for postoperative antibiotic treatment was 6 days (range 1-7 days, mean 5.6 days).

Correspondingly, in the case of mandibular angulus fracture, all but two respondents who treated similar fractures surgically reported antibiotic use as part of the treatment (37 of 39, 94.9%). Those who reported prescribing antibiotics as part of the surgical treatment of mandibular angulus fractures did so in conjunction with surgery. Thirty-three of 37 respondents (89.2%) favored antibiotic administration immediately after the fracture diagnosis, whereas the remaining respondents reported beginning antibiotic administration in conjunction with surgery. Postoperative prescription of antibiotics was practiced by 32 (86.5%) respondents. The median reported duration for postoperative antibiotic treatment was 5 days (range 3-7 days, mean 5.6 days). Most of the respondents favored chlorhexidine mouth rinse postoperatively. Treatment practices of the respondents are shown in Tables 2 and 3.

Table 2. Treatment strategies of 41 surgeons treating mandibular symphysis fractures

	No. of re- spondents	Yes n (%)	No n (%)		
Do you prescribe antibiotics as part of the treatment?	41	39 (95.1)	2 (4.9)		
Do you prescribe antibiotics as part of the treatment immediately after diagnosis of fracture?	39	36 (92.3)	3 (7.7)		
Do you prescribe antibiotics as part of the treatment in conjunction with surgery?	39	39 (100.0)	0 (0)		
Do you prescribe antibiotics as part of the treatment postoperatively?	39	34 (87.2)	5 (12.8)		
Do you recommend chlorhexidine as a part of postop- erative treatment?	41	37 (90.2)	4 (9.8)		
		Mean (range)	Median		
What is your duration of choice for postoperative antibiotic treatment (days)?	34	5.6 (1-7)	6		
What duration for post-operative chlorhexidine mouth rinse do you recommend to patients (days)?	37	8.6 (5–14)	7		
		0-12h	13-24h	24-48h	≥49h
		n (%)	n (%)	n (%)	n (%)
In what timeframe do you strive to operate a similar fracture?	41	4 (9.8)	25 (61.0)	12 (29.3)	0 (0)

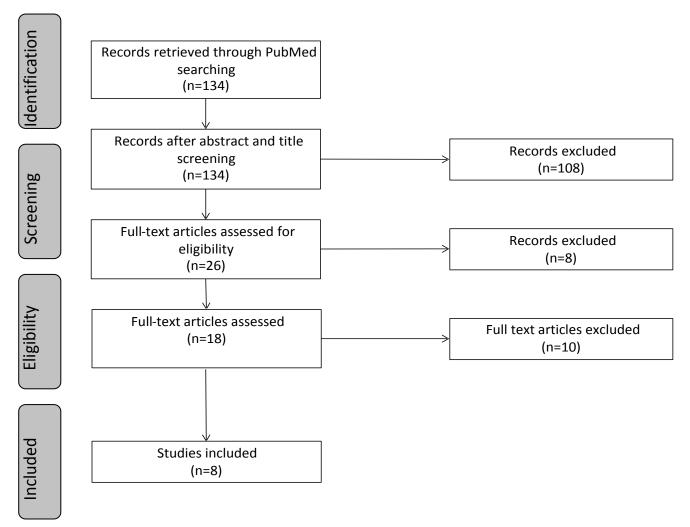


Fig 3. A flow chart of study selection

When asked about the antibiotic of choice, no clear differences were found in antibiotic protocols

between the two cases. The antibiotic of choice immediately after diagnosis and postoperatively

Table 3. Treatment strategies of 39 surgeons treating mandibular angulus fractures

	No. of re- spondents	Yes n (%)	No n (%)		
Do you prescribe antibiotics as part of the treatment?	39	37 (94.9)	2 (5.1)		
Do you prescribe antibiotics as part of the treatment immediately after diagnosis of fracture?	37	33 (89.2)	4 (10.8)		
Do you prescribe antibiotics as part of the treatment in conjunction with surgery?	37	37 (100.0)	0 (0)		
Do you prescribe antibiotics as part of the treatment postoperatively?	37	32 (86.5)	5 (13.5)		
Do you recommend chlorhexidine as a part of postop- erative treatment?	39	35 (89.7)	4 (10.3)		
		Mean (range)	Median		
What is your duration of choice for postoperative antibiotic treatment (days)?	32	5.6 (3-7)	5		
What duration for post-operative chlorhexidine mouth rinse do you recommend to patients (days)?	35	8.7 (5–14)	7		
		0-12h n (%)	13-24h n (%)	24-48h n (%)	≥49h n (%)
In what timeframe do you strive to operate a similar fracture?	39	3 (7.7)	20 (51.3)	16 (41.0)	0 (0)

(in descending order) was penicillin (G or V), aminopenicillin (ampicillin or amoxicillin), and cephalosporin (first or second generation). Furthermore, penicillin was the most commonly prescribed antibiotic perioperatively followed by cephalosporin and aminopenicillin, which were both equally favored. Metronidazole or clavulanic acid was combined with the above antibiotics in some cases. Antibiotic choices are presented in the Table 4.

Literature review

Figure 3 presents a flowchart of study selection. The remaining articles were assessed for eligibility. Four of the included studies were prospective and four were retrospective. Two of the prospective studies were both randomized and placebo controlled. All studies were published between 2001 and 2017. According to the studies, restricting antibiotic exposure to a maximum of 24 hours postoperatively was not related to a higher risk of SSIs. No articles demonstrated a benefit of prolonged postoperative antibiotic therapy. Additionally, according to one retrospective study (10), the length of time between an injury of the angle of the mandible and the first dose of antibiotic given is statistically significant; patients who received their first dose of antibiotic over 72 hours after the injury had a threefold higher rate of postoperative infection than those who received antibiotics between 24 and 72 hours after the injury. Table 5 summarizes the major parameters of the included studies.

DISCUSSION

The aim of the present study was to assess the use of antibiotics by oral and maxillofacial surgeons in mandibular fracture patients. We hypothesized that treatment practices may vary and that evidencebased treatment recommendations are required.

Our hypothesis was confirmed. The survey showed notable differences in antibiotic use practices between surgeons, particularly with preoperative use and duration. However, responses were consistent on the use of perioperative antibiotic prophylaxis; those who prescribe antibiotics as part of the surgical treatment of mandibular angulus or symphysis fractures do so in conjunction with surgery. Particularly interesting was that two of the respondents reported not prescribing antibiotics at all as part of the surgery. No significant differences were found in the antibiotic practices between the two fracture types.

Prophylactic use of antibiotics as part of the surgical management of mandibular fractures, especially in the dentate part of the mandible, seems to be compulsory due to a possible risk of contamination with oral microbes. However, there is no clear protocol for prophylactic antibiotic treatment. According to previous studies, surgeons use often longer courses of prophylactic antibiotics in the surgical treatment of mandible fractures than the current literature deems necessary (2).

In our survey, the median duration of postoperative antibiotic treatment was 5 days in the case of mandibular angulus fracture and 6 days in the case of symphyseal fracture. Thus, half of the respondents favored an antibiotic duration of nearly a week. The literature review of this study revealed that restricting antibiotic exposure to a maximum of 24 hours postoperatively was not related to a higher risk of SSIs. A systematic review by Shridharani et al. (13) revealed that an antibiotic regimen exceeding 24 hours postoperatively is not needed in patients treated with open reduction and internal fixation. According to our survey, antibiotic practices of oral and maxillofacial surgeons are not in concordance with the previous research evidence of mandibular fractures.

The similar trend has been observed previously. Administration of antibiotics varies extensively among surgeons in previous studies. For example, in a study by Lovato and Wagner (6), the duration of postoperative antibiotic treatment in the surgical management of mandibular fractures ranged from

Table 4. Antibiotic choice in fractures involving the angle and symphysis of the mandible

		No. of re- spondents	Penicil- lin G/V	Cephalo- sporin (1st or 2nd gen.)	1	Metronidazole or cla- vulanic acid combined with other antibiotics
			n (%)	n (%)	n (%)	n (%)
Symphysis	after diagnosis	36	29 (80.6)	3 (8.3)	4 (11.1)	11 (30.6)
fracture	in conjunction with surgery	39	27 (69.2)	6 (15.4)	6 (15.4)	13 (33.3)
	postoperatively	34	27 (79.4)	2 (5.9)	5 (14.7)	9 (26.5)
Angulus	after diagnosis	33	25 (75.8)	3 (9.1)	5 (15.2)	11 (33.3)
fracture	in conjunction with surgery	37	25 (67.6)	6 (16.2)	6 (16.2)	13 (35.1)
	postoperatively	32	25 (78.1)	1 (3.1)	6 (18.8)	7 (21.9)

Authors (year)	Study design	No. of analyzed patients	Antibiotics used preoperatively	Antibiotics used perio- peratively	Antibiotics used postoperatively	Duration of post- operative antibiotics	Study groups	Infection rate between groups
Ham- mond <i>et</i> <i>al.</i> (2017) (10)	Retrospective audit	642	Amoxicillin/ clavulanic acid (Augmentin® 1.2 g IV three times daily from admission until the operation)	Augmentin® 1.2g IV if patient had not had a dose within the previ- ous 8 h	Augmentin® 625 mg orally three times daily for a total of 5 days.	5 days	First dose of antibiotic between 24 and 72 h after fracture of the angle of the mandible <i>vs.</i> 72 h between injury and the first dose of antibiotic	8.0% vs. 23.7% No significant difference in infection rate be- tween antibiotic regimens
Gaal <i>et al.</i> (2016) (7)	Retrospective cohort study	510	Surgeon's discretion	Surgeon's discretion	Surgeon's discretion	Not reported	Perioperative antibiotic <i>vs.</i> perioperative and preoperative antibiotic OR perioperative and postoperative antibiotic	8.6% <i>vs.</i> 16.6%**
Domingo <i>et al.</i> (2016) (11)	Retrospective review	358	Surgeon's discretion	Surgeon's discretion	Surgeon's discretion	1 day- over 7 days	Preoperative antibiotic only vs . preoperative and postoperative antibiotic	10.2% <i>vs</i> . 14.1%**
Singh <i>et al.</i> (2013) (3)	. Regional 2-stage prospective audit	302	Stage 1: Surgeon's discretion Stage 2: amoxicillin 500 mg and metronidazole 500 mg given IV every 8 h on admission	Stage 1: Surgeon's discretion Stage 2: amoxicillin 500 mg and metronidazole 500 mg given IV every 8 h on admission	Stage 1: Surgeon's discretion Stage 2: two postoperative doses of amoxicillin 500 mg and metronida- zole 500 mg given IV	Stage 1: 3–5 days Stage 2: 1 day	Preoperative and perioperative antibiotic and 1-day postop- erative antibiotic regimen <i>vs</i> . preoperative and perioperative antibiotic and 3–5 days postop- erative antibiotic regimen	8.9% vs. 10.3%**
Schaller <i>et</i> <i>al.</i> (2013) (4)	Prospective, single center, randomized, double blind, placebo controlled clinical trial	59	1- and 5-day(s) groups: amoxicillin/ clavulanic acid 1.2 g IV every 8 h from admission until 24h postoperatively	1- and 5-day(s) groups: amoxicillin/clavulanic acid 1.2 g IV every 8 h from admission until 24h postoperatively	1-day group: Amoxicillin/ clavulanic acid 1.2 g IV every 8h until 24h postoperative- ly and oral placebo every 8 h for another 4 days. 5-day group: amoxicillin/ clavulanic acid 1.2 g IV until 24 h postoperatively AND amoxicillin/ clavulanic acid 625 mg orally every 8 h for another 4 days.	1 day-5 days	Preoperative and perioperative antibiotic and 1-day postopera- tive regimen <i>vs.</i> preoperative and perioperative antibiotic and 5 days postoperative antibiotic regimen.	20.7% vs. 20.0%**
Lovato and Wagner (2009) (6)	I Retrospective chart review	150	Surgeon's discretion	Surgeon's discretion	Surgeon's discretion	1 day- 10days	Perioperative antibiotic (no more than 24 h of antibiotics in the postoperative period) <i>vs.</i> extended regimen postoperative antibiotic (anywhere from 24 h to 10 days of antibiotics in the postoperative period)	13.3% vs. 10.7%**
Miles <i>et al.</i> (2006) (8)	Prospective randomized trial	181	Surgeon's discretion	Postoperative antibiotic group: Cefazolin 2 g	Postoperative antibiotic group: Peni- cillin G 2.4 mIU (intramuscular)	Depot penicillin was used	Preoperative and perioperative antibiotic vs. preoperative and perioperative and postoperative antibiotic	14.0% vs. 9.9%**
Abubaker and Rollert (2001) (12)	Prospective, randomized, double-blind clinical study	30	All patients: Penicil- lin G IV 2 million U every 4 h	All patients: Penicillin G IV 2 million U every 4 h	All patients: Penicillin G IV 2 million U every three times. Group 1: Penicillin VK orally, 500 mg every 6 h for five days. Group 2: oral placebo for five days	5 days	Preoperative, perioperative and 12 h postoperative antibiotic. Oral placebo. vs. preoperative, periop- erative antibiotic and 5-day regi- men of postoperative antibiotic	12.5% vs. 14.3%**

Table 5. Summary of literature research of mandibular fractures and antibiotic use

IV - intravenously; * - three times higher rate of postoperative infections; ** no statistically significant difference.

24 hours to 10 days in an extended antibiotic regimen group. Several antibiotics were used, including cephalosporins, penicillin, amoxicillin/clavulanic acid, and clindamycin. The same trend was also revealed in a retrospective study by Domingo *et al.* (11). Active discussion should address the unnecessarily protracted durations of antibiotic regimens.

According to a systematic review by Kyzas (2), the antibiotic of choice varies widely in previous studies. Penicillins, aminopenicillins, and cephalosporins were the most commonly used types of antibiotics both in the systematic review by Kyzas (2) and in the responses in our survey. However, the choice of antibiotic regimen was at the surgeon's discretion in several of the studies in the literature review. This may distort the results and lead, for example, to a situation where antibiotics are prescribed especially for the patients assumed to be at a higher risk of infection.

The benefit of perioperative antibiotics has been shown previously. In a systematic review, Andreasen et al. (5) reported that short-term antibiotic prophylaxis is indicated to reduce infection rates as part of the treatment of compound mandibular fractures. They observed an approximately fourfold reduction in infection rates and recommended a single-dose or 1-day prophylactic antibiotic therapy. In the present study, in addition to perioperative antibiotic administration, most surgeons reported prescribing antibiotics for the waiting period prior to surgery. Hammond *et al.* (10) found that the period between an injury of the angle of the mandible and the first dose of antibiotic is statistically significant; patients who received their first dose of antibiotic over 72 hours after the injury had a threefold higher rate of postoperative infections than those who received antibiotics between 24 and 72 hours after the injury. Therefore, it may be concluded that antibiotic treatment is justifiable while waiting for surgery, especially in mandibular angle fractures.

There is no apparent evidence that omitting antibiotic treatment would increase the risk of postoperative infections in patients awaiting surgery. Nevertheless, it is understandable that surgeons want to protect patients by prescribing an extended antibiotic regimen against postoperative infections, which may be severe and lead to revision surgery and the need for a larger surgical approach. However, prolonged prophylactic antibiotics should be reserved for patients susceptible to infection complications. Several factors may influence the risk of complications. Smoking history, alcohol abuse, poor oral hygiene, systemic illness, or an infected tooth in line with the fracture may predispose to infections and delayed healing (14,15). The timeframe for surgery of a mandibular angulus or symphysis fracture was consistent in our survey; all respondents strove to operate similar fractures within 48 hours. Hurrell *et al.* (16) observed in their prospective study that it may be safe to delay the treatment of mandible fractures. They did not find a statistically significant association between outcome and treatment delay. The mean delay was 4.6 days (range 0–41 days) in the study. Even though treatment delay does not increase postoperative infection risk significantly, it should be noted that merely stabilizing the mobile and often painful fracture and accelerating recovery are valid reasons for prompt treatment.

As part of the survey, we asked about the use of chlorhexidine mouth rinse postoperatively in mandibular fracture treatment. About 90% of the respondents recommended it postoperatively to their patients (median duration 7 days, range 5–14 days in both fracture types). While local chlorhexidine is beneficial in oral surgery procedures, there is still lack of evidence on the optimal duration of treatment (17). Preoperative chlorhexidine mouth rinse is beneficial in preventing bacteremia in oral surgery (18). Thus, chlorhexidine rinsing is also useful preoperatively, which could be particularly suitable for a fracture population in which oral cleansing prior to fracture surgery may be deficient.

Our study has some limitations. First, the number of survey respondents was quite small (n=41) and thus we did not reach all suitable oral and maxillofacial surgeons. Secondly, conclusions of the literature research remained limited. Four studies in the literature review were retrospective and only two of the four prospective studies were both randomized and placebo controlled. In addition, there were few patients (n=30) in the prospective, randomized, double-blind clinical study by Abubaker and Rollert (12). Common practices would also provide a better basis for retrospective studies. There is a further need for prospective, multicenter, randomized control trials.

CONCLUSIONS

In conclusion, evidence-based guidelines for antibiotic treatment as part of the surgical management of mandibular fractures are needed at both the international and unit levels. Based on the current literature, we recommend perioperative and 1-day postoperative prophylactic antibiotic prophylaxis as part of the surgical treatment of non-complicated and non-comminuted mandibular fractures of the dentate region. Additionally, antibiotic treatment may be appropriate prior to surgery,

STATEMENT OF CONFLICT OF INTEREST

The authors state no conflict of interest.

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APPENDIX

Literature review search query: (((Mandibular[MeSH Terms] AND (fracture[Title/Abstract] OR trauma[Title/Abstract] OR trauma[MeSH Terms])) OR (mandible fracture[MeSH Terms])) AND ((antibiotics[Title/Abstract]) OR prophylaxis[Title/Abstract])).

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