Efficacy of amoxicillin/clavulanic acid in preventing infectious and inflammatory complications following impacted mandibular third molar extraction

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Objective. To find out whether the frequency of postoperative infectious and inflammatory complications (IC) in subjects treated with placebo (Pl) is greater than those treated with antibiotic (Ab) after extraction of an impacted mandibular third molar (M3). Our hypothesis is there are more IC in Pl than in Ab, with a maximum ratio difference of 0.067.
Study design. A double-blind placebo-controlled randomized clinical trial. The sample was derived from the population of subjects attending Cruces Hospital for evaluation and extraction of 1 M3 under local anesthesia. Patients were treated with postoperative placebo or amoxicillin/clavulanic acid 500/125 mg 3 times a day during 4 days. The outcome variable was infectious and inflammatory complications. Sex, age, smoking, molar depth, angulation, need for sectioning, ostectomy, and operation time were recorded. Analysis was by intention to treat, risk measures, and logistic regression.
Results. In 490 subjects (259 Ab and 231 Pl), the frequency of IC was 1.9% in the Ab and 12.9% in the Pl group (OR 7.6, 95%CI 2.9-19.9; $P < .001$). The number needed to treat was 10 (7-16). Unadjusted relative riskwas 0.15 (0.06-0.38) ($P < .001$). Absolute reduction risk was 0.11(0.066-0.155)]. Therefore, the hypothesis cannot be rejected. Multivariate analysis shows treatment with antibiotic (OR = 8.66 (3.17-23.67); $P < .001$) and age (OR = 1.08 (1.00-1.16); $P = .029$) are the only variables to be included in the logistic regression model.
Conclusion. Amoxicillin/clavulanic acid is efficacious in reducing the incidence of IC following third molar extraction but should not be prescribed in all cases.
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The incidence of infectious and inflammatory complications (IC) following an impacted mandibular third molar (M3) extraction varies between 0% and 45%, according to different published studies[1-16] Controversy exists over the use of systemic antibiotics for its prevention. While there is some evidence that antibiotics can reduce the incidence of postoperative complications,[2-4,9,10,14,15,17,18] there is equally convincing evidence to the contrary.[1,5-7,11-13,16,19,20] As the Cochrane Library has published, better evidence is needed regarding the use of antibiotic prophylaxis in patients undergoing tooth extraction.[21]

The specific aim of this study was to assess the efficacy of amoxicillin/clavulanic acid 500/125 mg in preventing infectious and inflammatory complications (IC) in M3 subjects using a double-blind placebo-controlled randomized clinical trial. Our hypothesis was that the occurrence of IC was greater in patients treated with placebo (Pl) than in those treated with antibiotic (Ab), with a maximum ratio difference of 0.067.

Likewise we analyzed variables such as age, sex, smoking, molar depth and angulation, ostectomy, need for sectioning and intervention time to identify risk factors associated with post-operative IC.[8,10,22-26]

PATIENTS AND METHODS

The randomized clinical trial (RCT) was unicentric, prospective, placebo-controlled, and double-blinded of 2 parallel groups. The RCT was approved by the

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Table I. Characteristics of the control variables recorded for each of the groups

Variable	*Ab, n = 259*	*Pl, n = 231*	*Total, n = 490*	*P*	*Pl lost, n = 2*	*Ab lost, n = 2*
Age:				0.59[a]		
Mean	24.26	24.01	24.15		26.33	24.33
SD	5.1	4.89	5.01		2.56	2.58
Gender:				0.36[b]		
Man	99	98	197		1	1
Woman	160	133	293		1	1
Smoking, cigs/day:				0.43[c]		
None	160	139	295		1	0
0-10	65	62	127		1	0
11-20	31	30	61		0	2
>20	3	4	7		0	0
Depth type*:				0.13[c]		
II	85	70	155		2	0
III	107	82	189		0	1
IV	67	79	146		0	1
Angulation:				0.93[c]		
vertical	77	64	141		1	0
mesioangular	85	82	167		0	0
distoangular	21	19	40		0	2
horizontal	76	66	142		1	0
Intervention time, sec**:				0.84[a]		
mean	517.21	522.03	519.5		330.5	832.5
SD	276.29	255.78	266.56		13.4	378.3
Sectioning				0.32[b]		
No	120	96	216		1	0
Yes	139	135	274		1	2
Ostectomy***:				0.03[c]		
None	14	6	20		0	0
1/3	208	170	378		2	2
2/3	34	50	84		0	0
3/3	3	5	8		0	0

Ab, Subjects treated with antibiotic; *Pl,* subjects treated with placebo.
*Type II: totally covered by soft tissue and without bone coverage; type III: totally covered by soft tissue and partially by bone; type IV: totally covered by bone.
**Time measured using chronometer, from commencement of incision to the cutting of the last suture, by an external observer.
***1/3: Between crown and dental neck; 2/3: between dental neck and 2/3 of roots; 3/3: between 2/3 of roots and apexes.
[a,b,c]*P,* statistical significance of the homogeneity tests between the groups Pl and Ab. a: Logistics regression; b: Fisher exact bilateral test; c: Pearson's bilateral chi square.

Cruces Hospital Ethics Committee and by the Spanish Medicines Control Agency under protocol no. 00-0314. All the patients taking part in the study fully understood its scope and signed the informed-consent form. Furthermore, they had a contact telephone number throughout the trial duration to manage concerns.

The study sample was derived from the population of subjects attending Cruces Hospital for evaluation and extraction of an M3 under local anesthesia. The study was carried out at the Maxillofacial Surgery Department of Cruces Public Hospital between March 2001 and February 2003. Healthy patients of both sexes were included. A single M3 was extracted from each patient.

Patients with any bacterial endocarditis risk factors were excluded, as were pregnant and breastfeeding women. Also excluded were patients with acute infections 10 days prior to the intervention and/or those who had had to take antibiotics; and those with a history of allergy or intolerance to the drugs used in this study.

Ab received amoxicillin/clavulanic acid 500/125 mg oral 3 times a day for 4 days after the intervention, and Pl received placebo.

To determine sample size, we considered that the difference in IC between Pl (10%) and Ab (3.3%) would be equal to or less than 0.067, which would be equal to a relative risk (RR) of 0.33. To test this hypothesis with a type I error of .05 with a power of 80%, we needed a final sample of 490 subjects. A sample of 540 subjects was randomized, calculating a 10% expected loss.

The simple randomization was performed using the C4-SDP program (Glaxo Biometry, Madrid, Spain) and each of the enrolled patients was assigned the corresponding blinded random successive treatment number, which was used as the patient's number.