Relationship between Timing of Antibiotic Administration and Complications Following Surgical Extraction of Lower Third Molars

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Abstract

Aim: The aim of this prospective clinical trial was to evaluate the effects of antibiotic therapy following different administration times on the postoperative complications of surgical removal of lower impacted third molars.

Materials and Methods: Three hundred and twenty seven consecutive patients (128 males and 199 females) aged 18 to 40 years old (mean=23.1±3.9 years) were recruited into this study. The lower third molars of all recruited patients were surgically extracted. Participants received either intravenous Velocef 1 gram or intra-oral 500 mg Cephalexin pre- (Group A, n=122), pre- (Group B, n=70) or post-operatively (Group C, n=135). Immediate and late complications following the surgery; including pain, swelling, trismus, paraesthesia, bleeding, dry socket, infection and fracture of mandible; were assessed 3 days and 7-14 days following the surgery.

Results: The most frequent complications were slight pain, swelling, and trismus. The most frequent complications were associated with post-operative antibiotic administration and least complications were associated with pre-operative antibiotic administration (p=0.000). Post-operative administration of antibiotic was associated with more pain (r=0.186, p=0.001), swelling (r=0.181, p=0.001), trismus (r=0.277, p=0.000), and dry socket (r=0.335, p=0.000).

Conclusions: Following surgical extraction of third molars, preoperative antibiotic administration is more effective in reducing the post-surgical complications than pre-operative antibiotic administration which in turn is more effective than post-operative antibiotic administration.

Keywords: Antibiotic, Third Molar, Complications after Extraction.

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Introduction

The surgical extraction of lower third molars is the most common intervention in oral surgery.[1] It is usually coupled with considerable post-operative complications that have biological and social impacts. [2, 3]

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Complications include dysaesthesia, infection, fracture of mandible, dry socket, pain, swelling, trismus, hemorrhage, damage to adjacent teeth, and displaced teeth. [4, 5]

The use of antibiotics in the existence of an ongoing infection is not in dispute. [6]

However, the efficacy of antibiotics in the prevention of postoperative infection for cases in which third molars are removed is still controversial. Some studies are against the use of antibiotics and showed no benefit of prescribing them for third molar surgery. [7-12]

On the other hand, some studies reported significant effects of antibiotics in the reduction of post-operative complications following third molar surgery. [13- 15]

The use of antibiotics is still thought to affect the occurrence of complications after third molar surgical removal. [4, 5] Different antibiotics were used following third molar extraction including tetracyclins, penicillins, metronidazole, lincomycin, neomycin, azithromycin, cephalosporins among others.

The most frequent form of antibiotic prophylaxis in third molar surgery is still systemic administration, although antiseptic mouthwashes and locally administered antibiotics are effectively used to prevent postoperative infection.

Intravenous route for antibiotic administration is also used for third molar surgery. [14, 16]

Foy et al. (2004) concluded that intravenous administration of antibiotics before third molar surgery could improve clinical recovery in healthy adult patients with the presence of risk factors that might suggest delayed recovery such as having the third molars below the occlusal plane. [16]

Antibiotic treatment might decrease pain, swelling, or trismus; and improve wound healing.[6,13-15,17-18]

Some researchers suggested that antibiotics reduce infections following third molar surgery but should not be prescribed in all cases and are not recommended for routine use. [19]

With the current advances in the contemporary standards of antibiotic prophylaxis in dentistry, it is important to monitor antibiotic use and prescription among dental practitioners as well as facilitate continuing education for practitioners regarding the public health risks related to the over-prescription of antibiotics. [20]

In a meta-analysis and review of literature, Schwartz and Larsen (2007) concluded that overall, many studies were inadequate and of poor quality because they suffered flaws such as small sample sizes, no control groups and insufficient statistical power to avoid type II, or false-negative errors. [20]

Consequently, clinicians would profit from knowing whether it is clinically appropriate to use an effective antibiotic therapy for third molar surgery. Also, patients would not sustain the risk of pharmacological over-treatment or side effects. Therefore, further studies are still required in this regard.

The aim of this prospective clinical trial was to evaluate the effects and efficacy of antibiotic therapy using different administration routes and times on the postoperative complications of surgical removal of lower impacted third molars.

Patients and Methods

Three hundred and twenty seven consecutive patients (128 males and 199 females) were recruited into the study from patients who attended the oral and maxillofacial surgery department at Jordan University Hospital, Amman, Jordan for surgical extraction of lower third molars. Patients were 18 to 40 years old (mean=23.1±3.9 years).

An invitation to participate in the study was extended to the patients. Each participant was provided with a full explanation of the study and

an informed consent was obtained from each participant before being recruited into the study.

One investigator conducted all clinical and radiographic examinations and thoroughly assessed each patient before and after third molar surgical extraction. The assessment included patients' dental and medical histories, complaints, and personal information including name, age, gender, education, occupation, address and marital status. Patients with any medical problem were excluded from the study. Only patients with fully impacted third molars that are partially or fully covered with bone were recruited into this study.

Intra examiner reliability was performed on 25 duplicate examinations using Kappa statistics. Kappa was 0.94 indicating substantial agreement as examination criteria were very clear and simple.

The lower third molars of all recruited patients in this study were surgically extracted by the same surgeon who was an experienced consultant in Oral and Maxillofacial surgery. Non-traumatic surgical approach was adopted during the removal of all third molars. The extracted teeth were removed by simple elevation following the removal of bone from around and height of the contour of tooth and tooth division. This technique ensured reducing trauma levels to the minimum.

The study population was randomly distributed into 3 groups matched by age and gender. Group A included patients who received pre-operative antibiotic cover, group B included patients who received peri-operative (at the start of the operation) antibiotic cover, and group C included patients who received post-operative antibiotic cover. Patients who went under sedation received peri-operative antibiotic cover, while patients who had no sedation received either pre- or post-operative antibiotic cover after being randomly allocated to either group A or C.

All patients received antibiotic treatment (either intravenous Cephradine 1 gram or oral 500 mg Cephalexin) before, during (at the start of the operation) or after the surgery. Patients received intravenous antibiotic if they went under sedation while they received oral antibiotic if they had no sedation.

After surgery, the immediate and late complications of the surgery were assessed.

The assessed complications included pain, swelling, trismus, paraesthesia, bleeding, dry socket, infection and fracture of mandible. The immediate complications were assessed during the first 3 days following the surgery and late complications were assessed 7-14 days later according to Siddiqi et al. (2010). [12]

Statistical Analysis

The data were analyzed using the SPSS computer software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc., Chicago, IL, USA). The association between the variables was analyzed using the Chi-Square test, while the linear regression analysis was used to predict complications using the timing of antibiotic administration. For all statistical analysis, the significance level was set at $P \leq 0.05$.

Results

One hundred and four patients had only one lower third molar to remove (60 patients with left lower third molar and 44 patients with lower right third molar), while 223 patients had both their right and left third molars extracted. In total, 267 lower right third molars and 283 lower left third molars were extracted.

Preoperative antibiotic cover was given to 122 patients, pre-operative antibiotic cover was given to 70 patients, while 135 patients received post-operative antibiotic.

The most frequent immediate complications were slight pain, swelling, and trismus. Patients' immediate complications are summarized in Table (1).

The most frequent late complications were also slight pain, swelling, and trismus. However, 187 patients recorded no late complications at all. Late complications are summarized in Table (2).

Correlations

Immediate complications were significantly related to the time of antibiotic administration (Chi square test degree of freedom (df) = 10, p=0.000). More frequent immediate complications were associated with post-operative antibiotic administration.

Late complications were significantly related to the time of antibiotic administration (Chi square test degree of freedom (df) = 26, p=0.000). The most frequent late complications were associated with post-operative antibiotic administration and least complications were associated with pre-operative antibiotic administration.

When each late complication was considered individually, the following significant relations were identified using Pearson correlation: Post-operative administration of antibiotic was associated with more pain (r=0.186, p=0.001), swelling (r=0.181, p=0.001), trismus (r=0.277, p=0.000), and dry socket (r=0.335, p=0.000).

Linear regression analysis showed that the time of antibiotic administration was very successful in predicting late complications following third molar surgical extraction (R=0.599, p=0.000), as well as predicting the occurrence of immediate swelling (R=0.451, p=0.015) and immediate trismus (R=0.537, p=0.022).

Comparison of Groups According Timing of Antibiotic Administration

Using ANOVA test to compare the complications according the timing of antibiotic administration; significant differences were identified between the three groups in regard to late pain, late swelling, late trismus, and late dry socket (p= 0.001, 0.001, 0.000, and 0.000, respectively). (Table 3)

In order to identify the exact relationships between each pair of individual groups, the Post Hoc LSD statistical test was used (Table 4) and the following relationships were identified. Immediate swelling when antibiotics were pre-operatively administered was significantly less than that detected when antibiotics were pre-operatively administered (p=0.039), which in turn was significantly less than that detected when antibiotics were administered post-operatively (p=0.022).

On the other hand, late pain was significantly more reported in post-operative group when compared to pre-operative (p=0.001) and pre-operative (p=0.003) groups. Furthermore, pre-operative group had significantly less late swelling when compared to both pre-operative and post-operative groups (p=0.002 and 0.001, respectively). In addition, post-operative group had more late trismus in comparison to both pre-operative and pre-operative groups (p=0.000 and 0.002, respectively). Finally, post-operative group had significantly more dry socket than pre-operative and pre-operative groups (p=0.000).

Table (1): Immediate complications associated surgical removal of lower third molar (n=327).

	Frequency	***Percent***
Slight pain	*24*	*7.3*
Slight pain and swelling	*22*	*6.7*
Slight pain, swelling and trismus	*165*	*50.5*
Slight pain and trismus	*11*	*3.4*
Moderate pain, swelling and trismus	*87*	*26.6*
Severe pain, swelling and trismus	*18*	*5.5*
Total	*327*	*100.0*

Table (2): Late complications associated surgical removal of lower third molar (n=327).

	Frequency	Percent
Slight pain	7	2.1
Slight pain and swelling	3	0.9
Slight pain, swelling and trismus	11	3.4
Slight pain and trismus	46	14.1
Slight swelling	2	0.6
Slight swelling and trismus	5	1.5
Slight swelling, trismus and numbness	1	0.3
Slight trismus	24	7.3
Slight pain, trismus and dry cocket	4	1.2
Slight trismus and dry socket	28	8.6
Dry socket	2	0.6
Dry socket "smoker"	5	1.5
Infected socket	2	0.6
No complications	187	57.2
Total	327	100.0

Table (3): ANOVA test to compare the complications according to the timing of antibiotic administration.

		df	Mean Square	F	Significance
Immediate Swelling	**Between Groups**	2	.278	2.935	.055
	Within Groups	324	.095		
	Total	326			
Immediate Trismus	**Between Groups**	2	.168	1.387	.251
	Within Groups	324	.121		
	Total	326			
Late Pain	**Between Groups**	2	1.182	7.198	.001
	Within Groups	324	.164		
	Total	326			
Late Swelling	**Between Groups**	2	.443	7.311	.001
	Within Groups	324	.061		
	Total	326			
Late Trismus	**Between Groups**	2	3.258	13.943	.000
	Within Groups	324	.234		
	Total	326			
Late Dry Socket	**Between Groups**	2	2.511	27.744	.000
	Within Groups	324	.091		
	Total	326			

Table (4): Post Hoc LSD (Least Significant Difference) test for comparison of complications between pairs of groups according the timing of antibiotic administration.

Dependent Variable	Compared Groups	Mean Difference	Standard Error	Significance	95% Confidence Interval	
					Lower Bound	Upper Bound
Immediate Swelling	A versus B	.10	.046	.039*	.00	.19
	A versus C	-.01	.038	.821	-.08	.07
	B versus A	-.10	.046	.039*	-.19	.00
	B versus C	-.10	.045	.022*	-.19	-.02
	C versus A	.01	.038	.821	-.07	.08
	C versus B	.10	.045	.022*	.02	.19

Immediate Trismus	*A versus B*	*.09*	*.052*	*.103*	*-.02*	*.19*
	A versus C	*.02*	*.043*	*.669*	*-.07*	*.10*
	B versus A	*-.09*	*.052*	*.103*	*-.19*	*.02*
	B versus C	*-.07*	*.051*	*.194*	*-.17*	*.03*
	C versus A	*-.02*	*.043*	*.669*	*-.10*	*.07*
	C versus B	*.07*	*.051*	*.194*	*-.03*	*.17*
Late Pain	*A versus B*	*.00*	*.061*	*.939*	*-.11*	*.12*
	A versus C	*-.17*	*.051*	*.001**	*-.27*	*-.07*
	B versus A	*.00*	*.061*	*.939*	*-.12*	*.11*
	B versus C	*-.18*	*.060*	*.003**	*-.29*	*-.06*
	C versus A	*.17*	*.051*	*.001**	*.07*	*.27*
	C versus B	*.18*	*.060*	*.003**	*.06*	*.29*
Late Swelling	*A versus B*	*-.11*	*.037*	*.002**	*-.19*	*-.04*
	A versus C	*-.10*	*.031*	*.001**	*-.16*	*-.04*
	B versus A	*.11*	*.037*	*.002**	*.04*	*.19*
	B versus C	*.01*	*.036*	*.771*	*-.06*	*.08*
	C versus A	*.10*	*.031*	*.001**	*.04*	*.16*
	C versus B	*-.01*	*.036*	*.771*	*-.08*	*.06*
Late Trismus	*A versus B*	*-.09*	*.072*	*.201*	*-.24*	*.05*
	A versus C	*-.31*	*.060*	*.000**	*-.43*	*-.19*
	B versus A	*.09*	*.072*	*.201*	*-.05*	*.24*
	B versus C	*-.22*	*.071*	*.002**	*-.36*	*-.08*
	C versus A	*.31*	*.060*	*.000**	*.19*	*.43*
	C versus B	*.22*	*.071*	*.002**	*.08*	*.36*
Late Dry Socket	*A versus B*	*.02*	*.045*	*.586*	*-.06*	*.11*
	A versus C	*-.24*	*.038*	*.000**	*-.32*	*-.17*
	B versus A	*-.02*	*.045*	*.586*	*-.11*	*.06*
	B versus C	*-.27*	*.044*	*.000**	*-.35*	*-.18*
	C versus A	*.24*	*.038*	*.000**	*.17*	*.32*
	C versus B	*.27*	*.044*	*.000**	*.18*	*.35*

A: Pre-operative antibiotic group, B: Peri-operative antibiotic group, C: Post-operative antibiotic group, *Significant relation (p≤ 0.05).

Discussion

Prophylactic antibiotics have been prescribed to reduce the possibility of postoperative local complications following third molar extraction.

This study reported a significant difference among the different groups where pre-operative antibiotics were associated with less immediate and late complications than pre-operative antibiotics, which in turn was associated with fewer complications than post-operative antibiotics.

After the surgical removal of lower third molars, the postoperative oral prophylactic antibiotic treatment was less effective in reducing immediate and late complications than pre- and pre- operative antibiotic administration, and therefore is not recommended for routine use. This concurs the results of previous studies.[21-23]

The findings of this study are consistent with the established principles of systemic antibiotic prophylaxis, which state that the systemic antibiotic should be present in the tissue before starting the procedure [24] and that use of post-surgical antibiotics has no advantage. [25]

Furthermore, the axiom of antibiotic prophylaxis is to provide an adequate drug level in the tissues before, during, and for the shortest time possible after the surgical procedure to prevent or reduce the incidence of postoperative infection. [26, 27]

Once surgery has been completed, antibiotics are no longer justified since they do not lessen any of the postoperative clinical symptoms. [21]

Rout and Frame (1992) found out that a single intravenous bolus injection of cefuroxime provided satisfactory alveolar bone concentrations for routine antibiotic prophylaxis at the time of wisdom tooth removal. [23] Adequate concentration of cephradine (Velosef) in serum and mandibular bone was reported in patients undergoing third molar surgery following a single 1 g intravenous injection. [28]

The strength of our report is that it is the only study with large numbers of patients that evaluated all patients pre- and post-operatively and that the analyzed complications by comparison were of different timing of antibiotic regimens.

Most articles involved either small numbers of patients in prospective studies or larger numbers in retrospective studies, none of which stated whether the patients were all seen postoperatively. [6]

Unfortunately, comparison of the published studies represents a tremendous challenge because of the variability in parameters and methods used for each study. [29]

It does worth to suggest that the frequency of complications following surgical removal of third molars might be associated with other variables such as surgical techniques and state of eruption of third molars. Every attempt was made during this study to standardize such factors by following atraumatic surgical technique and removal of fully impacted third molars that were fully or partially covered by bone. Further studies are required to study the effects of other factors on post- operative complications following the surgical extraction of lower third molars.

Conclusions

Following surgical extraction of lower third molars, preoperative antibiotic administration is more effective in reducing the post-surgical complications than pre-operative antibiotic administration which in turn is more effective than post-operative antibiotic administration.

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العلاقة بين توقيت إعطاء المضادات الحيوية والمضاعفات التي تلي الإستصال الجراحي للأضراس الثالثة السفلى

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الملخص

الهدف: هدفت هذه التجربة السريرية إلى تقييم آثار العلاج بالمضادات الحيوية التي تلي أوقات إعطاءها في أوقات مختلفة على المضاعفات المحتملة بعد الاستئصال الجراحي للأضراس الثالثة السفلى.

المواد والطرق: تمت دراسة 327 مريضاً ومريضة (128 ذكور و199 إناث) الذين تتراوح أعمارهم بين 18 سنة و 40 سنة (متوسط العمر= 23.1 ± 3،9 عاما). تم إستئصال الأضراس الثالثة السفلى جراحيا لجميع المرضى الذين تلقوا المضادات الحيوية إما عن طريق الوريد على شكل غراماً واحداً من فيلوسيف أو عن طريق الفم على شكل 500 ملغ من السيفاليكسين قبل العملية (مجموعة أ عدد المرضى= 122) ، وأثناء العملية (المجموعة ب، عدد المرضى= 70) أو بعد العملية (المجموعة ج، عدد المرضى= 135). كانت المضاعفات الفورية والمتأخرة التالية للجراحة هي: الألم والتورم، وصعوبة فتح الفم، والنزيف، والعدوى وكسر في الفك السفلي، وجميعها قيمت 3 أيام وبين 7-14 يوماً التالية للعملية الجراحية.

النتائج: كانت المضاعفات الأكثر شيوعا الألم الخفيف، والتورم، وصعوبة فتح الفم. وارتبطت أكثر المضاعفات المتكررة مع إعطاء المضادات الحيوية بعد الجراحة وارتبطت المضاعفات الأقل مع إعطاء المضادات الحيوية قبل العملية.

كان إعطاء المضادات الحيوية عند الاستئصال الجراحي للأضراس الثالثة السفلى قبل الجراحة الأكثر فعالية في الحد من المضاعفات الجراحية، وأكثر فعالية من إعطاء المضادات الحيوية بعد العمليات الجراحية.

الكلمات الدالة: المضادات الحيوية، الضرس الثالثة، المضاعفات بعد الإستصال الجراحي.