Efficacy of antibiotic prophylaxis on third molar extraction

Eficácia da profilaxia antibiótica na extração de terceiros molares


*aUFU – Universidade Federal de Uberlândia, Faculdade de Odontologia, Departamento de Periodontia, Uberlândia, MG, Brasil


Resumo

Introdução: Exodontia de terceiro molar é um procedimento odontológico comum, frequentemente desafiador, com complicações pós-operatórias aumentadas. A necessidade de profilaxia com antibióticos nesses casos ainda é motivo de debate. Objetivo: O objetivo deste estudo foi avaliar o efeito da profilaxia com antibióticos no curso clínico pós-operatório das cirurgias de extração do terceiro molar. Material e método: Sessenta e três pacientes foram randomicamente alocados em dois grupos posteriormente a cirurgia de exodontia dos quatro terceiros molares. Grupo ATB (N = 33) utilizou 1g de amoxicilina uma hora antes do procedimento cirúrgico e grupo CTR (N = 30) sem profilaxia antibiótica. Os dentes foram classificados de acordo com Pell & Gregory e Winter. Análises clínicas foram realizadas nos períodos de 3, 7, 14 e 30 dias após o procedimento cirúrgico. As análises consistiram na avaliação do edema, variação de abertura de boca e a cicatrização dos tecidos moles. Também foram executadas análises centradas nos pacientes por meio da aplicação da escala visual analógica (VAS) para avaliação de dor, inflamação, sangramento, dificuldade de abertura bucal e de mastigação. Resultado: Não houve diferenças entre os grupos em relação ao posicionamento dos dentes. Não foi observada influência da profilaxia antibiótica nos parâmetros clínicos de cicatrização, edema e abertura de boca. Os pacientes não notaram diferenças em relação ao seu conforto no pós-operatório. Conclusão: A incidência de complicações foi baixa e não foi relacionada a processos infecciosos. O uso de antibioticoterapia profilática não apresentou efeitos benéficos para o curso clínico pós-operatório em exodontia de terceiros molares.

Descritores: Antibioticoprofilaxia; cicatrização; terceiro molar.

Abstract

Introduction: Third molar extraction surgery is a common dental procedure, often challenging with increased post-operative complications. The need for antibiotic prophylaxis in these cases remains debated. Objective: The aim of this study was to evaluate the effect of antibiotic prophylaxis on the postoperative clinical course of third molar extraction surgeries. Material and method: Sixty-three patients were randomly allocated into two groups after extraction of the four third molars. ATB group (N = 33) the patients received 1g of amoxicillin one hour before the surgical procedure, CTR group (N = 30) the patients did not receive antibiotic prophylaxis. Clinical analyses were performed at 3, 7, 14, and 30 days after the surgical procedure. These analyses consisted of assessing oedema, variation in mouth opening, and soft tissue healing. Furthermore, patient-centered analyses were also carried out through the application of the visual analogue scale (VAS) to assess pain, inflammation, bleeding, difficulty opening the mouth, and chewing. Result: No influence of antibiotic prophylaxis was observed on the evolution of clinical parameters of healing, oedema, and mouth opening. Patients did not notice differences regarding their comfort during the postoperative period. Conclusion: The incidence of complications observed in the present study was low and was not related to infectious processes. The use of prophylactic antibiotic therapy has no beneficial effects on the postoperative clinical course in third molar extraction.

Descriptors: Antibiotic prophylaxis; healing; third molar.
INTRODUCTION

Third molar extraction surgeries are procedures routinely performed in clinical practice in Dentistry as a way to prevent or treat complications inherent to the maintenance of these teeth in the oral cavity, such as: caries, periodontal diseases, or odontogenic cysts. However, as the indications for extraction of these teeth may be related to their challenging position and late eruption, surgery can be challenging, due to the frequent need for osteotomies and odontosection techniques that can consequently lengthen the surgical time, and may increase the occurrence of post-operative morbidity.

The repair of post-extraction sockets after third molar extractions may be associated with inflammatory and infectious complications, such as trismus, edema, pain, speech and chewing difficulties, bruises, and changes in sensitivity in the operated areas arising from tissue trauma. In addition, in more severe cases, complications such as alveolitis and abscesses may occur. These complications can influence the decisions of professionals, some of whom indicate the use of antibiotics prior to the surgical procedure, because the most serious complications associated with the extraction of third molars are infectious processes.

However, most surgical procedures for third molar extractions occur in young individuals with good general health conditions. Additionally, this surgery is usually performed on an elective basis, in an uncontaminated surgical field. Despite these characteristics, inherent to this type of surgery, there is still a lack of knowledge about the real need to apply antibiotic prophylaxis for third molar extractions, as conflicting data are found in the literature. A systematic review of the literature, including 98 studies, that evaluated the use of antibiotic prophylaxis in various surgical procedures in the oral cavity indicated the need for antibiotic prophylaxis in third molar extraction. On the other hand, another systematic review indicated that the use of antibiotic prophylaxis has a debatable positive effect in third molar extractions, and highlighted the risk of bacterial resistance to antibiotics when indicating extensive antibiotic prophylaxis for all types of cases. There is still a clear need for clinical studies that add information about whether antibiotic prophylaxis exerts any kind of positive effect in the prevention of infectious surgical complications after third molar extractions.

Thus, understanding the requirement for the rational use of antibiotic prophylaxis therapy, particularly in view of the current scenario in which bacterial resistance is a real concern in all medical areas, the aim of the current study was to evaluate the effect of antibiotic prophylaxis with 1 gram of amoxicillin one hour before the surgical procedure in the postoperative clinical course of third molar extraction surgeries.

MATERIAL AND METHOD

Ethical Considerations

This study was approved by the Research Ethics Committee of the Federal University of Uberlândia (CAAE: 49164821.0.0000.5152). The study was conducted in accordance with the precepts of the Declaration of Helsinki, and previously registered in the Brazilian Registry of Clinical Trials (REBEC - U1111-1269-7450).

Study Design

The sample consisted of 67 (sixty-seven) healthy patients from the Faculty of Dentistry of the Federal University of Uberlândia. The study design was a parallel randomized, controlled trial following the CONSORT (Consolidated Standards of Reporting Trails) protocol. Patients were allocated into 2 groups according to the type of preoperative care protocol given to patients (n=67): CTR: No use of antibiotic prophylaxis (n = 32); ATB: Use of 1 g of antibiotic prophylaxis.
(Amoxicillin) 1 hour before surgery (n = 35). In the postoperative period, both groups used the same analgesic and anti-inflammatory protocols.

Sample Size Calculation

The sample size calculation for this study was based on the primary variable of pain sensation obtained by the visual analogue scale (VAS). Considering variations of 0.5 on the scale as being significant and having a mean standard deviation of 0.85 as a prediction\textsuperscript{10}, it was determined that a sample size of 30 patients per group would be enough for a β power greater than 0.90 with a type I error fixed at 0.05.

Eligibility Criteria

As inclusion criteria for the study, patients were required to present the following characteristics: Be over 18 years old, present good oral hygiene (plaque index <20%), present the four third molars. Patients with the following characteristics were excluded from this study: Patients with periodontal disease, patients with systemic diseases or conditions or who used drugs that alter bone metabolism (except compensated diabetics), decompensated diabetics (glycated haemoglobin above 8%), pregnant or lactating women, heavy smokers (above 10 cigarettes a day), the presence of periapical lesions, the presence of pericoronitis lesions.

Surgical Procedure

Initially, a clinical and panoramic radiographic examination was performed of all patients. Subsequently, the teeth were classified according to the Pell & Gregory and Winter classification. Preoperatively, patients in the ATB group received 1 g of amoxicillin, and both groups received 8 mg of dexamethasone 1 hour before surgery. The surgical procedure began with intra and extraoral antisepsis and asepsis. The sterilized surgical drapes were then positioned and local anaesthesia was performed using neural blockade techniques in the surgical areas. Subsequently, incisions, detachments, and extractions of dental elements were carried out using various instruments, after which the sutures were applied.

After the sutures, the patients received the same postoperative care protocol, being prescribed sodium diclofenac (50mg) for 3 days every 8 hours and sodium dipyrone (500mg) for 3 days every 6 hours. A mouthwash based on 0.12% chlorhexidine digluconate was prescribed for 7 days every 12 hours, and in the first 3 days the patient was instructed to place the liquid in their mouth and keep it in position without rinsing for 1 minute. From the fourth to seventh day, the patient was instructed to start rinsing the liquid. The sutures were removed 7 days after surgery.

Clinical Analysis

The patients were clinically analysed at 3, 7, 14, and 30 days after surgery, and the presence and area of oedema and soft tissue healing were measured. Analyses of pain, inflammation, bleeding, and difficulty opening the mouth and chewing were also performed by applying a VAS scale completed by the patients themselves.

The analysis of the oedema area was performed using two measurements on the face, perpendicular to each other: line A, distance between the gonion and the external palpebral commissure of the patient; line B, distance between the midpoint of the tragus and the labial commissure (Figure 1A). The variation in mouth opening was also measured, from the distance between the tops of the upper and lower central incisors with the patient in maximum comfortable mouth opening (Figure 1B). The analysis of soft tissue...
healing was measured based on 4 domains, valued on a scale of 1 to 3 according to the following observations: bleeding (1 – absence of bleeding; 2 – stimulated bleeding; 3 – spontaneous bleeding), tissue around the socket (1 - mucosa-like; 2 - <50% erythematous; 3 - >50% erythematous), suppuration (1 - no suppuration or plaque; 2 - presence of plaque; 3 - presence of suppuration), and colour and consistency of healing tissue (1 – close to normal pink or closed socket with no observed healing tissue; 2 – flaccid, reddish; 3 – brittle, greenish/greyish).

**Figure 1.** A) Scheme of the facial dimension evaluation where the following lines were traced bilaterally: line A, distance between the gonion and the external palpebral commissure; line B, distance between the midpoint of the tragus and the labial commissure; B) Scheme for evaluating the measurement of maximum mouth opening, which was measured by the distance between the tops of the upper and lower central incisors with the patient at maximum comfortable mouth opening.

For data collection on the VAS scale, a numerical visual scale was used with demarcated integers from 0 to 10, where 0 indicated an absence of complications and 10 an excess, which was observed for each patient: pain, inflammation/edema, haemorrhage/ bleeding, difficulty chewing, trismus.

**Statistical Analysis**

The GraphPad Prism 8.4 software (San Diego, CA, USA) was used to carry out the statistical analysis of this study. Normal distribution was confirmed of data from the analysis of facial dimensions and mouth opening, while data from the healing index and VAS scale were not distributed according to normality. The distribution of the numerical data of this study was evaluated using the Shapiro-Wilk normality test. The comparison between the CTR and ATB groups regarding facial dimensions and mouth opening was performed using the unpaired t-test. Longitudinal data within each group were evaluated using the ANOVA test for repeated samples complemented by Tukey’s post-test. The comparisons between the CTR and ATB groups of the healing index data and the VAS scale were performed using the Mann-Whitney test, while the longitudinal evaluation of these data within each group was performed using the Friedman test complemented by the Dunn’s test. The comparison between the position of the teeth prior to the surgical procedure between the groups was performed using the chi-square frequency test. All statistical tests were applied at a significance level of 5%.
RESULT

There Were no Differences Between the Groups Regarding the Position of the Teeth Before the Surgical Procedure

In total, 128 teeth were extracted from 32 patients who did not undergo antibiotic prophylaxis (64 upper teeth and 64 lower teeth), and 140 teeth were extracted from 35 patients who underwent antibiotic prophylaxis (70 upper teeth and 70 lower teeth). Two patients in each group did not attend follow-ups after the 7-day period and were excluded from this study (Figure 2). The teeth statistical analysis considered 30 patients who did not undergo antibiotic prophylaxis (120 teeth) and 33 patients who underwent antibiotic prophylaxis (132 teeth). When comparing the initial position of the teeth before the surgical procedure, no differences were observed between the groups in relation to Winter’s (Table 1) and Pell & Gregory’s classifications (Table 1).

Figure 2. Flowchart of the study.
Table 1. Frequency of third molar position according to Winter’s classification and to the Peel & Gregory classification

<table>
<thead>
<tr>
<th>Classification/Group</th>
<th>ATB Upper</th>
<th>CTR Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>Disto-angulated</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Mesio-angulated</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td>Horizontal</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>66</td>
</tr>
</tbody>
</table>

Peel & Gregory classification

<table>
<thead>
<tr>
<th>Classification/Group</th>
<th>ATB Upper</th>
<th>CTR Upper</th>
<th>ATB Lower</th>
<th>CTR Lower</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>32</td>
<td>28</td>
<td>30</td>
<td>27</td>
</tr>
<tr>
<td>B</td>
<td>16</td>
<td>28</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>C</td>
<td>18</td>
<td>10</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>66</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

Antibiotic Prophylaxis did not Influence the Evolution of Clinical Parameters of Healing and Oedema

There were no statistically significant differences between the groups regarding facial and mouth opening measurements, which are markers of the local inflammatory process (Table 2). In addition, no statistically significant differences were detected between the groups regarding the quality and evolution of post-extraction socket healing (Table 3). Progressive reduction in the oedema, return of the original opening of the mouth, and improvement in the patterns of healing were observed with the increase in the experimental period of analysis.

Table 2. Mean and standard deviation of facial dimensions and mouth opening during the follow-up of both groups

<table>
<thead>
<tr>
<th>Parameter/Period</th>
<th>3d</th>
<th>7d</th>
<th>15d</th>
<th>30d</th>
<th>3d</th>
<th>7d</th>
<th>15d</th>
<th>30d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ Horizontal Dimension (mm)</td>
<td>0.18±0.88</td>
<td>0.00±0.72</td>
<td>-0.21±1.73</td>
<td>-0.21±1.73</td>
<td>0.35±0.89</td>
<td>0.10±0.95</td>
<td>-0.03±1.23</td>
<td>-0.10±1.53</td>
</tr>
<tr>
<td>Δ Vertical Dimension (mm)</td>
<td>0.22±0.96</td>
<td>0.08±1.33</td>
<td>0.20±1.11</td>
<td>0.08±0.99</td>
<td>0.35±1.91</td>
<td>0.36±1.01</td>
<td>-0.12±2.12</td>
<td>-0.35±2.53</td>
</tr>
<tr>
<td>Δ Mouth opening (mm)</td>
<td>14.97±10.52</td>
<td>6.68±7.54</td>
<td>3.22±9.43</td>
<td>-0.01±6.22</td>
<td>19.67±8.90</td>
<td>10.57±8.42</td>
<td>3.72±7.05</td>
<td>1.65±5.48</td>
</tr>
</tbody>
</table>

Table 3. Median and interquartile interval of the healing index analysis assessed during the follow-up of both groups

<table>
<thead>
<tr>
<th>Period</th>
<th>Group</th>
<th>ATB</th>
<th>CTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3d</td>
<td>Upper Molar</td>
<td>5.75(4.50;7.00)</td>
<td>5.00(4.12;5.87)</td>
</tr>
<tr>
<td>7d</td>
<td>4.50(4.00;4.00)</td>
<td>4.00(4.00;4.00)</td>
<td>5.00(4.50;7.00)</td>
</tr>
<tr>
<td>15d</td>
<td>5.00(4.50;6.12)</td>
<td>4.25(4.00;5.00)</td>
<td>4.00(4.00;4.00)</td>
</tr>
<tr>
<td>30d</td>
<td>4.50(4.00;5.50)</td>
<td>4.00(4.00;5.00)</td>
<td>4.00(4.00;4.00)</td>
</tr>
</tbody>
</table>

Patients did not Notice Differences in Using or Not Using Antibiotic Prophylaxis in Relation to their Comfort During the Postoperative Phase

When evaluating the patient-centered parameters, no statistically significant differences were observed between the groups (Table 4). It was also possible to notice progressive improvement in the comfort reported by the patients with the increase in the follow-up period, and most patients did not show any more signs of discomfort on the 15th day of the postoperative period.
### Table 4. Median and interquartile interval of patient-centered analysis assessed by the VAS scale

<table>
<thead>
<tr>
<th>Group</th>
<th>3d.</th>
<th>7d.</th>
<th>15d.</th>
<th>30d.</th>
<th>3d.</th>
<th>7d.</th>
<th>15d.</th>
<th>30d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>2.50 (1.50;4.00)</td>
<td>1.50 (0.00;3.00)</td>
<td>0.00 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>4.25 (2.00;5.00)</td>
<td>2.00 (0.75;4.25)</td>
<td>0.50 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>2.00 (0.50;4.50)</td>
<td>0.00 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>2.00 (0.00;4.00)</td>
<td>0.00 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>0.00 (0.00;0.00)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>3.50 (2.00;6.00)</td>
<td>1.00 (0.00;3.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>5.00 (2.00;6.50)</td>
<td>2.00 (1.00;3.75)</td>
<td>0.00 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
</tr>
<tr>
<td>Chewing</td>
<td>5.00 (3.00;7.00)</td>
<td>2.00 (0.50;4.00)</td>
<td>0.00 (0.00;1.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>6.00 (5.00;8.00)</td>
<td>3.50 (1.50;5.25)</td>
<td>0.00 (0.00;1.50)</td>
<td>0.00 (0.00;0.00)</td>
</tr>
<tr>
<td>Mouth Opening</td>
<td>5.00 (2.50;7.00)</td>
<td>1.50 (0.00;3.00)</td>
<td>0.00 (0.00;2.00)</td>
<td>0.00 (0.00;0.00)</td>
<td>6.00 (5.00;7.12)</td>
<td>2.50 (1.25;3.50)</td>
<td>0.00 (0.00;1.50)</td>
<td>0.00 (0.00;0.00)</td>
</tr>
</tbody>
</table>

**In Both Groups the Incidence of Complications Was Low and Not Related to Infectious Processes**

The occurrence of 18 complications was observed during the postoperative period throughout the study, 7 of which occurred in the group where antibiotic prophylaxis was given and 11 in the group where antibiotic prophylaxis was not given. In the group that underwent antibiotic prophylaxis, 6 cases of trismus and one case of alveolitis were observed. All cases of trismus were treated by means of myofascial detachment, irrigation of the dental sockets with 0.12% chlorhexidine, and administration of 1g of dipyrone while there was pain. The case diagnosed as alveolitis was treated by irrigation of the dental alveolus of teeth 48 and 38 between the 7th and 15th day after the surgical procedure, associated with the use of dipyrone at 1g for 2 days. At the end of the study, all complications observed in this group were resolved.

In the group in which the patients did not undergo antibiotic prophylaxis, there was 1 case of hematoma associated with the lower teeth, 7 cases of trismus, 1 case of pain at the post-extraction site, and two cases of paresthesia. In the case of the hematoma, the patient was advised to apply heat therapy for 2 days and an improvement in the clinical picture was observed. This complication was isolated and was not accompanied by other types of symptoms. The cases in which trismus was diagnosed were treatments with myofascial detachment that were carried out within 7 days in two cases and within periods of 7 and 15 days in another two cases, and in all cases the patients were instructed to use dipyrone at 1g while there were painful symptoms. The case of exacerbated pain was associated with the post-extraction socket of tooth 38, which was irrigated with 0.12% chlorhexidine over a period of 7 days, after which the patient was instructed to use sublingual toragesic (ketorolac trometamol) for 2 days. Two patients with paresthesia associated with extraction of lower molars were treated with laser therapy sessions with a red laser (10 sessions, twice a week) and in one patient a total return of sensitivity was observed, while in another a partial return was observed. All complications were resolved within one month of follow-up. It is noteworthy that all these complications were related to lower molar teeth that were in a horizontal position or mesio-angulated in position B or C.

**DISCUSSION**

In general, the present study demonstrated that the use of antibiotic prophylaxis in immunocompetent patients has no impact on the reduction in complications after third molar extraction procedures. The tissue healing process depends on the inflammatory process and antibiotic prophylaxis does not seem to impact this phenomenon enough to promote clinically significant differences. Thus, the null hypothesis of this study was accepted.

It was not possible to observe infectious conditions during the study and the observed complications were of an inflammatory nature. There were no statistically significant differences between the groups in relation to oedema and difficulty in opening the mouth, and a progressive improvement in this condition was observed during the period of analysis, indicating the
beginning of an inflammatory process and its spontaneous resolution over the course of the postoperative period. Thus, it is possible to state that the use of antibiotic prophylaxis did not affect the formation of oedema and clinical signs of limited mouth opening and trismus, as demonstrated in previous clinical studies\textsuperscript{12,13}. The position of the teeth before the third molar extraction is one of the factors that has the greatest impact on the clinical outcome and the occurrence of postoperative complications\textsuperscript{3}. Thus, it is worth mentioning that in our study there were no differences between the groups in terms of surgical complexity, as demonstrated by the similarity in the position of the teeth between the two groups. It is important to note that the surgical procedure was performed by professionals with a high level of experience, which may have contributed to the low occurrence of complications\textsuperscript{14}. However, a clinical study showed that even patients undergoing third molar extractions performed by professionals with different levels of experience did not benefit from antibiotic prophylaxis\textsuperscript{15}. The suggestion that antibiotic prophylaxis is capable of preventing infectious events may have arisen considering protocols used for immunosuppressed patients or those with alterations that lead to an increased risk of infection\textsuperscript{5,8}. A study that evaluated patients treated at oral and maxillofacial surgery clinics in the United States reported a reduction of up to 40\% in inflammatory complications with the use of antibiotics. This conflicting result can be explained by factors highlighted by the authors, such as the non-standard application of different antibiotic prophylaxis therapy protocols. In addition, the parameters considered as complications were different from those used in our study (e.g., dry socket or surgical site infection) and the selection of patients was not random. Thus, other factors that could have an influence on postoperative complications may not have been controlled (e.g., the need for osteotomy and odontosection, duration of surgery, position of teeth, and influence of different levels of operator)\textsuperscript{5,16}. However, this and other studies suggest greater caution in the prophylactic use of antibiotics in third molar extraction surgeries due to the lack of beneficial effects of this therapy in the postoperative management of patients\textsuperscript{13,17,18}. It is important to highlight that the present study included healthy patients without acute inflammation or infection, which may influence the effectiveness of antibiotic prophylaxis therapy. The involvement of different levels of surgical complexity in the sample may have masked a possible effect of the use of antibiotics, as adjunctive treatments usually have more effect in more complex surgical conditions\textsuperscript{19,20}. Another limiting factor is that the sample calculation was based on a surrogate outcome (pain) that does not necessarily result in a postoperative complication in all cases\textsuperscript{3,19}. It is worth noting, as a positive point, that the sample size was large enough to assess the impact of different therapies on an outcome that is a precursor or a result of the main inflammatory or infectious complications associated with third molar extractions.

CONCLUSION

It can be concluded that the use of prophylactic antibiotic therapy does not have beneficial effects on the postoperative clinical course in third molar extraction, regardless of the initial position presented by the tooth. Therefore, according to the results obtained in the study, the use of prophylactic antibiotic therapy in this type of surgery should be limited.

AUTHOR CONTRIBUTIONS

Conceptualization: Oliveira GJPL, Pereira DA; Data curation: Oliveira GJPL, Mendes PGJ; Formal Analysis: Oliveira GJPL; Funding acquisition: Oliveira GJPL; Investigation Mendes PGJ, Pereira DA, Bonatto MS, Soares Júnior EC, Santos SS, Martins AVB; Methodology: Mendes PGJ, Pereira DA,
FUNDING

This study was financed by the Brazilian agencies CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico, 426954/2018-1), and FAPEMIG (Fundação de Apoio a Pesquisa do Estado de Minas Gerais - APQ-02211-21).

REFERENCES


CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

*CORRESPONDING AUTHOR

Guilherme José Pimentel Lopes de Oliveira, Av. Pará, 1760-1844, Umuarama, 38405-320 Uberlândia, MG, e-mail: guilherme.lopesoliveira@ufu.br

Received: November 7, 2023
Accepted: November 7, 2023