Knowledge and clinical decisions of Colombian dentists about the risk of osteonecrosis of the jaws in patients receiving treatment for osteoporosis

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INTRODUCTION

Maxillary osteonecrosis (ONJ) is a rare severe adverse reaction to drugs used to treat osteoporosis and cancer, such as bisphosphonates and denosumab. This complication consists of the progressive destruction of the mandibular and/or maxillary bone, with exposure of the necrotic bone in the oral cavity, which occurs more frequently with the use of antiresorptive agents in cancer and multiple myeloma1,2.

The risk of ONJ with bisphosphonates and denosumab in osteoporosis therapy is very low, close to 0.01%, as it is a low-dose and short-exposure therapy, unlike when they are used in cancer patients, with a risk of around 1.3%3,4. The prevalence of ONJ in patients receiving long-term oral bisphosphonate therapy was reported to be 0.1% (10 cases per 10,000), which increased to 0.21% (21 cases per 10,000) in patients older than 4 years. bisphosphonate exposure4.
Although the risk of ONJ is very low with the use of bisphosphonates and denosumab in osteoporosis, dental professionals still perceive a high risk of presenting this complication. They frequently request authorization for dental procedures to the prescribing physician, leading to dental complications due to delays in carrying out the procedures or associated with the suspension of treatment for osteoporosis6,7.

This study aims to ascertain the degree of knowledge and the clinical decisions that Colombian dentists make regarding ONJ risk associated with the use of bisphosphonates and denosumab in osteoporosis.

**METHODS**

A survey was designed to assess two areas. The first related to the level of knowledge of dentists regarding the risk of developing ONJ with bisphosphonates and denosumab evaluated with general questions about the topic. The second involved the clinical decisions made by professionals, which was assessed with hypothetical clinical cases.

The survey development process initially included a focus group, in which a dental professional, a clinical psychologist and epidemiologist expert in qualitative research, a rheumatologist and two internal medicine residents took part. Some initial questions were proposed that were subsequently submitted to a group of experts for approval and correction. The resulting tool was applied to a group of 30 students in their final year of dentistry studies at the Pontificia Universidad Javeriana (Bogotá) as a pilot test, seeking to evaluate the ease of response and understanding. Their comments were taken into account to make the final adjustments to the survey prior to its application.

The survey was hosted in the SurveyMonkey program (Supplement 1) and sent to dentists, maxillofacial surgeons, periodontists and oral rehabilitation specialists, affiliated with the Colombian Odontological Federation, during the period from October 2019 to August 2020. They were invited to participate by sending registered email by each professional, up to a maximum of 3 times.

During the period from October 2019 to August 2020, 660 did not respond to the survey. 340 responded to the survey and of these 19 (5.5%) were excluded because they had no clinical practice in the last 12 months, 57 (16%) due to their exclusive practice with pediatric patients and 77 (22%) because they did not complete the survey. In total, the responses of 187 dentists were analyzed (algorithm 1). The median age was 42 years (interquartile range 39-45). The majority were women (70.2%), with a greater presence of dentists from Bogotá (56.2%). Table 1 shows the demographic characteristics of the group of dentists who took part in the study.

**Knowledge assessment**

When evaluating the risk of developing ONJ, 50.2% of the respondents considered that the use of BPs was an absolute contraindication for a major dental procedure, while 51.3% expressed the same opinion for denosumab. For minor procedures, 53.2% of those surveyed considered the use of bisphosphonates an absolute contraindication and 27.8% a relative contraindication to carry out the procedure. The percentages for the use of denosumab were 42% and 28.3%, respectively (figure 1).

41.2% considered that ONJ risk was the same for those receiving bisphosphonates compared to those receiving denosumab. 45% considered that the risk of developing ONJ is greater if bisphosphonates are administered orally. 50% considered that the risk of ONJ is the same in patients with cancer, compared to patients with osteoporosis receiving bisphosphonates or denosumab. 70% of dentists considered that the risk of ONJ increases with the time of exposure to bisphosphonates, and 50% with the time of exposure to denosumab. Regarding the question of the risk of developing ONJ with bisphosphonate compared to denosumab, 70% were not sure.

70% of dentists reported that less than 25% of patients in their clinical practice diagnosed with osteoporosis and 57.8% of these patients being treated with bisphosphonates or denosumab. Of the dentists surveyed, 76.4% have not dealt with any case of ONJ, and of those who had, only 16.9% were associated with osteoporosis. 41.6% are unaware of any document for diagnosing and managing osteonecrosis of the jaw.

**Algorithm 1. Selection of surveys of dentists**

- 1,000 dentists
- 660 did not respond to the survey
- 340 responded to the survey
- 187 surveys
- Those excluded:
  - 19 for not having a clinical practice in the last 12 months
  - 57 exclusive practice with pediatric patients
  - 77 for not completing the survey
Evaluation of clinical decisions

The hypothetical cases used and the clinical decisions that dentists would make in that situation are presented in table 2. Of the reported decisions, the following stood out:

For case 1 (65-year-old woman with hip fracture and osteoporosis treated with denosumab for a year who required an extraction), only 1.37% considered carrying out the extraction and 74.66% considered it necessary to request an extraction authorization from the referring physician in order to perform the procedure.

For case 2 (53-year-old man with a history of rheumatoid arthritis managed with methotrexate and leflunomide who requires endodontics), 42.47% would request an opinion from the referring physician.

For case 3 (60-year-old woman with osteoporosis managed with alendronate and pending dental implant), 3.42% considered carrying out the treatment without suspending the bisphosphonate and 43.84% would request authorization from the referring physician to endorse the procedure.

For case 4 (64-year-old woman with osteoporosis undergoing treatment with zoledronic acid who required tooth extraction), 4.1% considered carrying out the procedure without suspending the bisphosphonate and 62.3% would request authorization from the referring physician.

For case 5 (Patient with osteoporosis who is being managed with denosumab, of which he has received 3 doses, with telopeptide C levels at 0.05 ng/mL), 26.03% would postpone the procedure while waiting for the decreased levels of telopeptide C.

The subgroup analysis showed that a lower proportion of professionals with postgraduate studies considered the use of bisphosphonates a relative contraindication for carrying out minor procedures (43.4 vs 54.9%, p 0.021) (table 3). For the other clinical decisions, no significant differences were found, regardless of the years of experience, the level of education (complete undergraduate vs. postgraduate) or the city where the professional practice was carried out.

Discussion

Colombian dentists’ knowledge and attitudes regarding the risk of developing ONJ with the use of bisphosphonates and denosumab, in treating osteoporosis, were analyzed in our study. We found a high proportion of professionals had limited knowledge of the ONJ risk associated with bisphosphonates and denosumab. In this sense, they would make incorrect decisions regarding the scheduling time of major and minor procedures.

Our findings are similar to those reported in other countries, where a low level of knowledge regarding the subject was reported. A study published by R Al-Eid et al. shows the results of a survey of 74 dentists in Saudi Arabia in which 39.2% of the respondents were not familiar with the term ONJ and 54% had no knowledge regarding the diagnosis and treatment of ONJ; 44% were unsure whether to discontinue bisphosphonate therapy prior to tooth extraction. A 2017 survey of Mexican dentists by Vinitzky-Brener et al. showed that only
Table 2. Clinical cases concerning decisions taken by Colombian dentists about the use of bisphosphonates or denosumab due to the risk of ONJ, during major and minor dental procedures

<table>
<thead>
<tr>
<th>Evaluation of clinical decisions. Cases/Responses</th>
<th>Would request a written opinion from the referring rheumatologist, in which define the risk of ONJ and whether or not the dental procedure is authorized</th>
<th>Would advise the patient that the use of zoledronic acid is an absolute contraindication for this type of dental procedure and that it will not be performed</th>
<th>Would recommend suspending the treatment and restarting it according to its clinical evolution (closure of the surgical wound)</th>
<th>Would perform the dental procedure without stopping zoledronic acid</th>
<th>Would not perform the procedure since he receives treatment with methotrexate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Nº 1: Woman, 65 years old, hip fracture and osteoporosis, with denosumab. Consultation due to the appearance of a dental lesion that you consider requires an extraction, considering the risk of developing ONJ, would you propose:</td>
<td>74.6%</td>
<td>16.4%</td>
<td>7.53%</td>
<td>1.3%</td>
<td>---</td>
</tr>
<tr>
<td>Case Nº 2: A 53-year-old man with rheumatoid arthritis is managed with methotrexate and leflunomide and oral calcium. Requires endodontic treatment, taking into account the risk of ONJ and the patient's scenario, would you consider:</td>
<td>42.4%</td>
<td>0.6%</td>
<td>54.7%</td>
<td>20%</td>
<td>---</td>
</tr>
<tr>
<td>Case Nº 3: A 60-year-old woman with osteoporosis managed with alendronate 70 mg weekly for 18 months. She is scheduled to perform a dental implant and attends her consultation prior to the intervention. Regarding treatment with alendronate you:</td>
<td>43.0%</td>
<td>27.4%</td>
<td>20.5%</td>
<td>4.7%</td>
<td>---</td>
</tr>
<tr>
<td>Case Nº 4: Woman, 64 years old with osteoporosis with zoledronic acid, an extraction will be carried out and she comes to your consultation regarding treatment with zoledronic acid:</td>
<td>6.2%</td>
<td>16.4%</td>
<td>11.4%</td>
<td>4.1%</td>
<td>---</td>
</tr>
<tr>
<td>Case Nº 5: Patient with osteoporosis with three doses of denosumab scheduled for a dental implant, in previous consultations with two dentists, who have refused to carry out the procedure since the patient has C telopeptide levels of 0.05 ng/mL. Your opinion regarding patient's the clinical case would be:</td>
<td>42.4%</td>
<td>26.0%</td>
<td>27.4%</td>
<td>4.1%</td>
<td>---</td>
</tr>
</tbody>
</table>
Table 3. Subgroup analysis regarding clinical decisions of knowledge of Colombian dentists about the use of bisphosphonates or denosumab due to the risk of osteonecrosis

<table>
<thead>
<tr>
<th>Knowledge evaluation</th>
<th>Years of experience</th>
<th>Applied studies</th>
<th>Town</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less than 10 years %</td>
<td>More than 10 years %</td>
<td>p</td>
</tr>
<tr>
<td>Major procedures with BFs. Absolute contraindication</td>
<td>21.3</td>
<td>29.4</td>
<td>0.15</td>
</tr>
<tr>
<td>Minor procedures with BFs. Relative contraindication</td>
<td>11.7</td>
<td>16.4</td>
<td>0.88</td>
</tr>
<tr>
<td>Major DNS procedures. Absolute contraindication</td>
<td>18.7</td>
<td>32.6</td>
<td>0.82</td>
</tr>
<tr>
<td>Minor DNS procedures. It is not a contraindication</td>
<td>21.3</td>
<td>33.1</td>
<td>0.93</td>
</tr>
</tbody>
</table>

BFs: bisphosphonates; DNS: denosumab.

40.5% were aware of ONJ and only 24.6% were familiar with some type of bisphosphonate. Another study assessing the knowledge of dentists about ONJ associated with bisphosphonates carried out in Korea by Yoo et al., in 2010, reported that only 56.5% of those surveyed knew the term ONJ and 31.4% related it to bisphosphonate use. Similar findings were reported by Alhussain et al., in 2015 in a study conducted with Canadian dentists, where 60% of the respondents did not have sufficient knowledge about ONJ and 50% did not know how to manage it. This is the first study conducted to assess the knowledge and clinical decisions of Colombian dentists. Our study suggests that there is a lack of knowledge regarding the risk of ONJ in treating osteoporosis with bisphosphonates and denosumab. According to the American Association of Oral and Maxillofacial Surgeons (AAOMS) 2014 recommendations and the first Colombian Consensus of ONJ associated with medications of 2019, treatment with bisphosphonates or denosumab is not an absolute or relative contraindication. Furthermore, treatment should not be suspended to perform the dental procedure. However, the committee recognizes that there are limited data to support or refute the pharmacological vacation period for patients with osteoporosis treatment, but vacation therapy may be beneficial after prolonged exposure to treatment. This is based on the very low risk of ONJ in the context of osteoporosis, which is 0.01%, as demonstrated by the FREEDOM study, which evaluated the use of denosumab in 4,550 patients, where there were no ONJ cases. In the HORIZON study with 7,765 patients managed with zoledronic acid and followed up for 3 years, only one case of ONJ occurred.

50% of the dentists responded that the risk of ONJ is the same in patients with cancer compared to osteoporosis. Studies that have evaluated ONJ risk in both scenarios have shown a large difference in risk, which is 10 to 150 times higher in cancer compared to osteoporosis (0.1-1.5% vs 0.01%). Regarding knowledge of scientific documents for the prevention and management of patients with ONJ, 41% are unaware of document for ONJ treatment. There are two important documents for the diagnosing and treating ONJ, the Guide of the American Association of Oral and Maxillofacial Surgeon (AAOMS) of 2014 and the I Colombian Consensus of ONJ published in 2019. In the study by R Al-Eid et al., the authors reported that most respondents were unaware of the AAOMS guidelines. In the evaluation of attitudes carried out through clinical scenarios, in clinical cases 1 and 3 of patients with osteoporosis managed with denosumab and bisphosphonates, respectively, 74.66% and 43.84% would request an opinion from the referring physician to authorize the dental procedure. According to the AOMMS recommendations and the Colombian ONJ consensus, an assessment by the referring physician is not required to define dental treatment.

Furthermore, our study suggests that ONJ is a very low frequency disease in dentistry, as shown by the fact that 76.5% of those surveyed have not had any case of ONJ and 70.2% of dentists respondents have less than 25% of patients in their clinical practice diagnosed with osteoporosis. Of those patients with osteoporosis, 57.9% are treated with bisphosphonates and denosumab. Our study suggests that the respondents lack knowledge for decision-making regarding the risk of ONJ with the use of bisphosphonates and denosumab in treating osteoporosis.

This study has some limitations. The sample size was relatively small, which may not be representative of all dentists in our country. However, the study encompasses the highest number of dentists participating in knowledge assessment, compared with other previous studies that used a similar methodology.
The authors declare no conflict of interest.
### Annex 1

**Survey**

1. Have you had patients in the last 12 months?  
   a. Yes  
   b. No  

2. Does your clinical practice work exclusively with children under 18?  
   a. Yes  
   b. No  

3. Gender  
   a. Feminine  
   b. Masculine  

4. Age: years  

5. City of clinical practice  
   a. Bogota DC  
   b. Medellin  
   c. Cali  
   d. Barranquilla  
   e. Other cities  

6. Level of study attained  
   a. Undergraduate  
   b. Postgraduate  

7. Years of clinical practice:  
   a. Less than 10 years  
   b. More than 10 years  

**Knowledge evaluation:**

Note to start the survey: In the following survey, the term bisphosphonate refers to the following drugs: zoledronic acid, ibandronate, alendronate, risedronate. These drugs, such as denosumab, are therapeutic options for osteoporosis treatment.

1. When carrying out **major** dental procedures (exodontics, open-field surgical procedures) in patients with osteoporosis treated with **bisphosphonates**, the use of this type of medication is:  
   a. An absolute contraindication for the dental procedure  
   b. A relative contraindication for the dental procedure  
   c. It is not a contraindication  
   d. Not sure  

2. When carrying out **minor** dental procedures (root canal treatment, cleaning, prophylaxis, resins, amalgams and crowns) in patients with osteoporosis treated with **bisphosphonates**, the use of this type of medication is:  
   a. An absolute contraindication for the dental procedure  
   b. A relative contraindication for the dental procedure  
   c. It is not a contraindication  
   d. Not sure  

3. When carrying out **major** dental procedures (extractions, open-field surgical procedures) in patients with osteoporosis under treatment with **denosumab**, the use of this medication is:  
   a. An absolute contraindication for the dental procedure  
   b. A relative contraindication for the dental procedure  
   c. It is not a contraindication  
   d. Not sure  

4. When carrying out **minor** dental procedures (root canal treatment, cleanings, prophylaxis, resins, amalgams and crowns) in patients with osteoporosis treated with **denosumab**, the use of this medication is:  
   a. An absolute contraindication for the dental procedure  
   b. A relative contraindication for the dental procedure  
   c. It is not a contraindication  
   d. Not sure  

5. The risk of developing osteonecrosis of the jaw in patients with osteoporosis with the use of bisphosphonates compared to the use of denosumab is:  
   a. Higher*  
   b. Likewise  
   c. Less  
   d. Not sure
6. The risk of developing osteonecrosis of the jaw in patients with osteoporosis who receive bisphosphonates according to their route of administration is:
   a. Greater if administered intravenously than orally
   b. Greater if administered orally than intravenously
   c. Same regardless of route of administration*
   d. Not sure

7. The risk of developing osteonecrosis of the jaw in patients with osteoporosis receiving bisphosphonates:
   a. Increases in relation to the time of use of the bisphosphonate*
   b. It is not modified in relation to the time of use of the bisphosphonate
   c. Not sure

8. The risk of developing osteonecrosis of the jaw in patients with osteoporosis receiving denosumab:
   1. Increases in relation to the time of use of denosumab*
   2. It is not modified in relation to the time of use of denosumab
   3. Not sure

9. The risk of developing osteonecrosis of the jaw in patients with osteoporosis receiving bisphosphonates or denosumab compared to patients receiving these same therapies for cancer treatment is:
   a. Higher
   b. Less*
   c. Likewise
   d. Not sure

10. Are you aware of published scientific consensus documents for the prevention and management of patients with drug-induced osteonecrosis of the jaw?
    a. Yes*
    b. No

11. The risk of developing drug-induced osteonecrosis of the jaw in a patient with osteoporosis treated with bisphosphonates or denosumab is:
    a. 1 in 10 patients per year
    b. 1 in 100 patients per year
    c. 1 in 1,000 patients per year
    d. 1 in 10,000 patients per year*

12. Approximately, what percentage of patients in your clinical practice have a diagnosis of osteoporosis?
    a. Less than 25%
    b. From 25 to 50%
    c. More than 50%
    d. None

13. Approximately, what percentage of patients in your clinical practice have been diagnosed with osteoporosis and are being treated with bisphosphonates or denosumab?
    a. Less than 25%
    b. From 25 to 50%
    c. More than 50%
    d. None

14. How many cases of drug-induced osteonecrosis of the jaw have you seen in the last 12 months?
    a. No case.
    b. One case
    c. Between 2 to 5 cases
    d. Between 6 to 10 cases
    e. More than 10 cases

15. Of these seen cases of drug-induced osteonecrosis of the jaw, most were related to:
    a. Cancer treatment
    b. Treatment for osteoporosis
    c. Both alike
    d. Not sure
    e. Not seen any cases

16. Do you know if there is any diagnostic test to assess the risk of osteonecrosis of the jaw in patients receiving bisphosphonates or denosumab?
    a. Does not exist.
    b. Yes, it exists but they are useless*
    c. Yes, it exists and it is useful
    d. No
    e. In case your previous answer was options "b" or "c", please specify which diagnostic test(s) refers


Clinical cases—clinical decisions

1. 65-year-old woman, history of hip fracture and osteoporosis, treated with denosumab for 1 year [last application 1 month ago]. Consultation due to appearance of dental lesion that you consider requires extraction, considering the risk of developing ONJ, you would propose:
   a. Postpone the extraction until the effect of the medication ends (six months)
   b. Carry out the extraction as there is no contraindication for the procedure*
   c. Request a written concept from the treating rheumatologist, in which the risk of ONJ is defined and whether or not the dental procedure is authorized
   d. Advise the patient that the use of denosumab is an absolute contraindication for this type of dental procedure and will not be carried out

2. A 53-year-old man with a history of rheumatoid arthritis managed with methotrexate 10 mg/week and leflunomide 20 mg daily, does not use glucocorticoids. His rheumatologist also prescribed oral calcium at his last visit. He requires endodontic treatment, taking into account the risk of ONJ and the patient’s scenario, you:
   a. Would not carry out the procedure as the patient is treated with methotrexate
   b. Would not carry out the procedure as the patient is treated with leflunomide
   c. Would carry out the procedure as there is no documented ONJ risk with the use of these medications*
   d. Would request a written concept from the treating rheumatologist, in which the risk of ONJ is defined and whether or not the dental procedure is authorized

3. A 60-year-old woman with a history of osteoporosis managed with alendronate 70 mg weekly for 18 months. She is scheduled to perform a dental implant and attends her consultation prior to the intervention. Regarding treatment with alendronate, you:
   a. Would perform the dental procedure without discontinuing alendronate*
   b. Would recommend suspending the treatment and restarting it according to its clinical evolution (closure of the surgical wound)
   c. Would explain that it is not a dental emergency and I would wait a 6-month cleaning time to perform the intervention
   d. I would advise the patient that the use of alendronate is an absolute contraindication for this type of procedure and will not be performed
   e. Would request a written concept from the treating rheumatologist, in which the risk of ONJ is defined and whether or not the dental procedure is authorized

4. A 64-year-old woman with a history of osteoporosis who has been managed with zoledronic acid 5 mg intravenously every year for two years, is scheduled for the next application in two months. The patient will undergo an extraction and attends your consultation prior to the intervention. Regarding treatment with zoledronic acid you:
   a. Would carry out the dental procedure without stopping zoledronic acid*
   b. Would recommend suspending the treatment and restarting it according to its clinical evolution (closure of the surgical wound)
   c. Would explain to him that it is not a dental emergency and I would wait a year for cleaning to carry out the intervention
   d. Would advise the patient that the use of zoledronic acid is an absolute contraindication for this type of dental procedure and will not be performed
   e. Would request a written concept from the treating rheumatologist, in which the risk of ONJ is defined and whether or not the dental procedure is authorized

5. A patient comes to your consultation who wants a second dental opinion. The patient suffers from osteoporosis and as treatment has received three doses of denosumab in the last two years, she was scheduled to carry out a dental implant, however, in previous consultations with two dentists, they have refused to perform the procedure as the patient presents C telopeptide levels at 0.05 ng/mL. Your opinion regarding the clinical case of the patient:
   a. Would indicate that the procedure be carried out, since the levels of C telopeptide are not a contraindication*
   b. Would tell you not to have the procedure done, due to raised C telopeptide levels
   c. Would postpone the procedure, until C telopeptide levels decrease
   d. Would not make any recommendations as I do not know the relationship between C telopeptide levels and complications derived from the procedure