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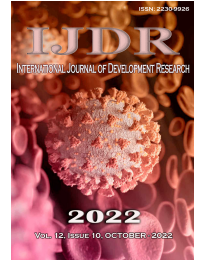
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REVIEW ARTICLE

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ASSOCIATION BETWEEN MAXILLARY SINUSITIS AND PERIAPICAL DISEASES: A SYSTEMATIC REVIEW

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ABSTRACT

Objectives: The purpose of this study was to systematically evaluate the evidence on the association between maxillary sinusitis and periapical diseases. **Methods:** An electronic search were performed of the Cochrane Library, PubMed, Embase and LILACS databases up to September 2020. The gray literature was also searched. Additional studies sought through hand searching of endodontic journals. Observational studies associating maxillary sinusitis with periapical diseases, diagnosed by radiography and/or computed tomography/CBCT were included. Risks of bias assessment and data extraction were performed. **Results:** Fourteen studies were selected and included in the qualitative analysis. Assessing methodological quality through the Checklist proposed by Downs and Black, most of the studies had scores below 0.50, not meeting most of the quality items. A meta-analysis cannot be performed due to the heterogeneity of the studies. According to the included studies, periapical diseases represented from 18% to 94.9% the etiology of odontogenic MS. **Conclusions:** Conflicting with other studies results, periapical diseases consisted the most frequent etiological factor associated with odontogenic MS.

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INTRODUCTION

Maxillary sinusitis consists of an inflammation of the maxillary sinuses which can be classified according to its duration, severity and etiology and is one of the most diagnosed pathologies in the world. Representing the fifth, most common condition for prescribing antibiotics and is associated with a significant negative impact on the quality of life of those affected (Huntzinger, 2007). The intimate relationship between the maxillary sinuses and the root apex of the posterior upper teeth is well known, which explains that odontogenic infections can cause the rupture of the Schneiderian membrane and develop changes in the maxillary sinuses (Kretzschmar, Kretzschmar JL, 2003; Lu Y et al., 1986; Melen I et al., 1986; Shanbhag et al., 2013). For this reason, it is particularly important to identify the etiology of MS to provide the appropriate treatment (Legert, Zimmerman, Stierna, 2003). Radiographs are important diagnostic tools for periapical changes and abnormalities of the maxillary sinuses. By contrast, they can cause overlapping of anatomical structures (Shanbhag et al., 2013; Brook, 2006; Nurbakhsh et al., 2003), as they are two-dimensional (2D) examinations of three-dimensional (3D) structures.

This does not occur in 3D examination modalities such as CT and cone beam CT, which can illustrate the degree of bone loss and the relationship between periapical lesions with MS (Hoskison et al., 2003; Nurbakhsh et al., 2003; Shanbhag et al., 2013). The association between sinusitis and odontogenic causes is well defined in the literature. However, there is no clarity between the association and risk factors for periapical diseases and maxillary sinusitis. Although this association is clear, it is sometimes neglected in clinical practice. To establish these criteria, a systematic review was conducted.

MATERIALS AND METHODS

Study Design: This systematic review is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Moher et al., 2009) (PRISMA) and registered on the PROSPERO database (CRD42020149674).

The research question was the following: What is the association between maxillary sinusitis and periapical diseases?

Search Strategy and Eligibility Criteria: Appropriate free-text key words and controlled vocabulary (MeSH terms) were used in the search strategies. The electronic search strategy was applied to the following databases up to September 2020: Cochrane Library, PubMed, EMBASE and Lilacs. Gray literature was searched through OpenGrey. ClinicalTrials.gov was searched for ongoing or recently completed clinical trials. A manual search was also performed to avoid missing relevant studies.

No language or date restriction was applied to any of the searches. The search strategy was performed using the terms “maxillary sinusitis”, “periapical diseases” and “odontogenic” combined by the Boolean operators AND/OR. The eligibility criteria were based on the Population, Exhibition, Comparison and Outcome criteria strategy, which included adults of 18 years or more with a diagnosis of MS (Population) comparing periapical disease as the cause of odontogenic MS (Exhibition) with other odontogenic factors (Comparison) to identify their association. Therefore, prospective, retrospective and cross-sectional studies that evaluated odontogenic factors as the cause of MS were included. Reviews, case reports, comment letters, letters to the editor, books, animal studies, studies including subjects younger than 18 years of age, studies using examination modalities other than radiography, CBCT or CT were excluded. The search strategy is shown in Supplemental file 1.

Study selection: Two reviewer authors (D.S.P. and J.B.S.J.) performed the study selection independently through the evaluation of the titles and abstracts of all studies identified in the electronic databases according to eligibility criteria. Full studies were retrieved and evaluated when their title and abstract did not provide enough information for a definite decision. Disagreements between the 2 reviewers at this stage were resolved by discussion with a third author (V.E.A.)

Quality Assessment: Selected studies were analyzed to verify their quality by two independent reviewers (D.S.P. and J.B.S.J.). If there was any disagreement at this stage, a third reviewer was requested (V.E.A.). The methodological quality of the included studies was evaluated by the Checklist proposed by Downs and Black (Downs, Black, 2009). This tool includes 27 items distributed into 5 subscales: 1) Reporting (09 items); 2) External validity (03 items); 3) Bias (07 items); 4) Confounding (06 items); 5) Power (01 item). Each of the 27 items were answered and scored 0 or 1, except for one item in the Reporting subscale, which scored 0 to 2, and the single item on power, which was scored 0 to 5. The total maximum score was 31. To assess answers to the 27 quality criteria, a score indicating the quality of the article was created, dividing the number of positive items by the total number of items evaluated.

Data Extraction and Synthesis of Evidence: The main characteristics of the included studies were extracted by two reviewers (D.S.P. and J.B.S.J.) and arranged into a data table. Even though most studies had the same primary objective, their methodologies differed regarding the diagnostic examination modality for diagnostic purpose and the subclassification of odontogenic etiologies of MS. The list of general characteristics of the selected studies is shown in table 1.

RESULTS

The search process screened 1169 references, published until September 2020. After the duplicates were removed, eligibility criteria were applied to 1149 articles. Forty studies were selected for full-text reading. After eligibility criteria application, 14 articles were selected for data extraction and qualitative analysis. The flowchart is present in Figure 1. The included studies were published between 1993 and 2019. These studies were carried out in Belgium (14), Brazil (15,16), Canada (17), Germany (18), India (19), Japan (20), Lithuania (21), Portugal (22), Sweden (23,24) and USA (25,26,27). Patient age ranged from 18 to 94 years (mean 49.31). Women represented 52.15% of the subjects, while men represented 47.85%. Evaluating the etiologies of odontogenic MS, most of the studies

showed endodontic factors as the most common cause, showing a prevalence ranging from 18% to 94.9% (Bajoria AA, Sarkar S, Sinha P. 2015; de Lima CO *et al.*, 2017; Guerra-Pereira I *et al.*, 2015; Shahbazian M *et al.*, 2009; Simuntis R *et al.*, 2017; Troeltzsch M *et al.*, 2015; Turfe Z *et al.*, 2019; Vestin FM *et al.*, 2017; Wang KL *et al.*, 2015; Yoshiura K *et al.*, 1993). Evaluating the prevalence of periodontal factors, only one study resulted in a higher prevalence of periodontal factors associated with odontogenic sinusitis, showing a percentage of 60% (Bomeli SR, Branstetter BF 4th, Ferguson BJ, 2009). The prevalence of other odontogenic factors has been reported in some studies. The presence of oroantral fistula represented 7.9% to 30% of the total odontogenic MS (Simuntis R *et al.*, 2017; Turfe Z *et al.*, 2019; Wang KL *et al.*, 2015; Yoshiura K *et al.*, 1993).

Three of the selected studies for qualitative analysis evaluated the prevalence of upper teeth involvement associated with odontogenic maxillary sinusitis. The most involved teeth were: maxillary first molar (31.6% -55%); maxillary second molar (33.3% -50%); maxillary second premolar (8% -11.6%); maxillary first premolar (3-7% -69%); canine (1.7%) and edentulous patients (1.67 %) (Simuntis R *et al.*, 2017; Turfe Z *et al.*, 2019). All these data, together with the main characteristics of the included studies, are shown in Table 2. The methodological quality of the studies was evaluated using the Downs and Black Checklist. Most of the studies had scores below 0.50, not meeting most quality items. The main methodological problems found were related to the external and internal validity of the studies, including the lack of a control group, lack of randomness and control of confounding factors (table 2).

DISCUSSION

In several studies included in this systematic review, between 51.8% - 82.3% of MS presented odontogenic causes (Bajoria AA, Sarkar S, Sinha, 2015; Guerra-Pereira *et al.*, 2015; Shahbazian *et al.*, 2009; Troeltzsch *et al.*, 2015; Turfe *et al.*, 2019; Wang *et al.*, 2015; Yoshiura *et al.*, 1993). These results were vastly different from data found in other included studies, in which the odontogenic cause ranged from 18.2% to 48% of the etiology of MS (Brazil. Ministério da Saúde, 2014; de Lima *et al.*, 2017; Maillet *et al.*, 2011; Mehra, Jeong, 2019; Vestin *et al.*, 2017). These results differ from reports of the literature in which the incidence of odontogenic MS was estimated between 10% and 12% of all cases of sinusitis (Maloney, Doku, 2019; Mehra, Jeong, 2019). Other odontogenic factors associated with MS were also evaluated. Several studies demonstrated periapical disease as the most common etiology among all odontogenic factors, representing 40% to 94%. These data are opposed to the study conducted by Troeltzsch M *et al.*, 2015, in which endodontic factors represented only 18% of the total odontogenic etiologies of MS. In this same study, iatrogenesis resulting from surgical procedures and dental implants were the odontogenic factors most associated with MS, representing 65%.

In the study conducted by Bomeli SR, Branstetter BF 4th and Ferguson BJ, 2009, periodontal disease was the most common etiological factor, representing 60% of the total odontogenic MS. In some studies, the presence of oroantral fistula constituted an etiological factor of odontogenic MS in 2.6% to 28% of the total number of the etiologies (Simuntis *et al.*, 2017; Turfe *et al.*, 2019; Yoshiura *et al.*, 1993; Wang *et al.*, 2015). Considering risk factors, several studies included in the qualitative analysis reported a greater association of odontogenic causes with unilateral MS (Turfe Z *et al.*, 2019; Vestin FM *et al.*, 2017; Yoshiura K *et al.*, 1993; Wang KL *et al.*, 2015). This association is corroborated in the study by Yoshiura K *et al.*, 1993, in which odontogenic MS was more frequent in young patients. In a study conducted by Wang KL *et al.*, 2015, 84% of the total odontogenic MS were unilateral. With the result obtained by Troeltzsch M *et al.*, 2015, the authors were able to conclude that most of the cases of unilateral MS (UMS) presented an odontogenic etiology.

16. If any of the results of the study were based on "data dredging", was this made clear?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18. Were the statistical tests used to assess the main outcomes appropriate?	1	1	1	1	1	1	1	1	1	1	1	1	1	0
19. Was compliance with the intervention/s reliable?	0	0	0	1	0	1	0	0	0	0	0	0	0	0
20. Were the main outcome measures used accurate (valid and reliable)?	1	1	1	1	1	1	1	1	1	1	1	0	1	1
Internal Validity - Confounding (selected bias)														
21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	1	1	1	1	1	1	1	1	0	1	0	0	1	1
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	0	0	0	0	1	1	0	0	0	0	0	0	0	0
23. Were study subjects randomized to intervention groups?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24. Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	0	1	0	0	0	0	0	0	0	0	0	0	0	0
26. Were losses of patients to follow-up taken into account?	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Power														
27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	0	1	1	1	1	1	0	1	0	1	0	1	0	1
	4	8	4	9	9	10	6	8	7	9	5	9	4	5
Quality Score: Answered items yes/total of items (27)	0,15	0,30	0,15	0,33	0,33	0,37	0,22	0,30	0,26	0,33	0,19	0,33	0,15	0,19

Association between maxillary sinusitis and periapical diseases: A systematic review

Statement of Clinical Relevance: Sinusitis is one of the most common respiratory diseases and presents different etiologies including odontogenic causes. The results of this systematic review highlighted periapical diseases as the most frequent etiologic factor associated with MS. Considering this fact, endodontic therapy may be the only choice for treating most cases of odontogenic MS.

Supplemental file 1. Search Strategy

Database	Search strategy
Cochrane	#1 #2 #3 #1 OR #2 #4 Periapical diseases #5 Odontogenic #6 #4 OR #5 #7 #3 AND #6 Maxillary sinusitis Rhinosinusitis
Lilacs	(tw:(maxillary AND (tw:(periapical diseases)) OR (tw:(odontogenic))) sinusitis))
Embase	maxillary sinusitis AND periapical diseases
Pubmed	maxillary sinusitis[Text Word] OR maxillary sinusitis[MeSH Terms] OR Sinusitis[Text Word] OR Sinusitis[MeSH Terms] OR Sinusitides[Text Word] OR Sinusitides[MeSH Terms] OR Sinus Infections[Text Word] OR Sinus Infections[MeSH Terms] OR Infection, Sinus[Text Word] OR Infection, Sinus[MeSH Terms] OR Infections, Sinus[MeSH Terms] OR Sinus Infection[Text Word] OR Sinus Infection[MeSH Terms] OR Maxillary Sinusitis[Text Word] OR Maxillary Sinusitis[MeSH Terms] OR rhinosinusitis[Text Word] OR rhinosinusitis[MeSH Terms] AND Periapical Diseases[Text Word] OR Periapical Diseases[Text Word] OR Disease, Periapical[Text Word] OR Diseases, Periapical[Text Word] OR Periapical Disease[Text Word] OR Periapical Disease[Text Word] OR Periodontitis, Periapical[Text Word] OR Periodontitis, Apical[Text Word] OR Apical Periodontitides[Text Word] OR Apical Periodontitis[Text Word] OR Periodontitides, Apical[Text Word] OR Periodontitis, Acute Nonsuppurative[Text Word] OR Acute Nonsuppurative Periodontitides[Text Word] OR Acute Nonsuppurative Periodontitis[Text Word] OR Nonsuppurative Periodontitides, Acute[Text Word] OR Nonsuppurative Periodontitis, Acute[Text Word] OR Periodontitides, Acute Nonsuppurative[Text Word] OR Periapical Abscess[Text Word] OR Dentoalveolar Abscess, Apical[Text Word] OR Abscess, Apical Dentoalveolar[Text Word] OR Abscesses, Apical Dentoalveolar[Text Word] OR Apical Dentoalveolar Abscesses[Text Word] OR Dentoalveolar Abscesses, Apical[Text Word] OR Periodontitis, Apical, Suppurative[Text Word] OR Periapical Periodontitis, Suppurative[Text Word] OR Periapical Periodontitides, Suppurative[Text Word] OR Periodontitides, Suppurative Periapical[Text Word] OR Periodontitis, Suppurative Periapical[Text Word] OR Suppurative Periapical Periodontitides[Text Word] OR Suppurative Periapical Periodontitis[Text Word] OR Alveolar Abscess, Apical[Text Word] OR Abscess, Apical Alveolar[Text Word] OR Abscesses, Apical Alveolar[Text Word] OR Alveolar Abscesses, Apical[Text Word] OR Apical Alveolar Abscess[Text Word] OR Apical Alveolar Abscesses[Text Word] OR Abscess, Periapical[Text Word] OR Abscesses, Periapical[Text Word] OR Periapical Abscesses[Text Word] OR Periapical Granuloma[Text Word] OR Granuloma, Periapical[Text Word] OR Granulomas, Periapical[Text Word] OR Periapical Granulomas[Text Word] OR Radicular Cyst[Text Word] OR periapical lesion[Text Word] OR odontogenic[Text Word]
Grey Literature	Maxillary sinusitis AND periapical diseases

In a study by Turfe Z *et al.*, 2019, only patients with UMS were evaluated. Among all cases of UMS, 45% of them were attributed to odontogenic causes. This association is extremely relevant because the referred professional can stick to patient's symptoms and suspect a possible odontogenic etiology when these symptoms occur, thus making it more feasible to refer the patient for appropriate treatment. It is well established in the literature that there is an intimate relationship between the maxillary sinuses and the root apices of the maxillary posterior teeth (Lu *et al.*, 1986; Melen *et al.*, 1986). Shahbazian M *et al.*, 2009, evaluated the proximity relationship between the upper posterior teeth and the floor of the maxillary sinus using periapical radiography and CBCT exams. The maxillary first and second molars showed an intimate relationship to the maxillary sinus floor in 50% and 45%, respectively, when using the CBCT. In this same study, it was demonstrated that periapical radiography was not accurate in determining this relationship, since among all the detected cases of the intimate contact of the teeth with the maxillary sinus by this bidimensional exam, only 58% were confirmed through the CBCT exam (Shahbazian *et al.*, 2009). This result is justified, since the periapical radiography consists of an examination that has limitations such as the overlapping of anatomical structures and does not demonstrate the real spatial perspective of the proximity of the dental roots to the maxillary sinus. According to Bajoria AA, Sarkar S, Sinha P, 2015 and Nunes CA *et al.*, 2017, the CBCT exam is extremely useful in the diagnosis and planning of odontogenic MS. Another study evaluated conventional CT exams for the diagnosis of odontogenic MS and this modality of image examination also proved to be an excellent tool in the diagnostic aid of odontogenic MS. Since CBCT has a good accuracy in the diagnosis of odontogenic MS and generates a much lower dose of ionizing radiation, this type of imaging exam may be more advantageous when compared to the CT (Guerra-Pereira *et al.*, 2015). Among the studies that evaluated the modalities of imaging exams, the study conducted by Simuntis *et al.*, 2017 stands out, which aimed to assess the ability of different professionals (endodontist, oral surgeon, general dentist, otolaryngologist and oral radiologist) to identify the odontogenic etiology of MS through CT exams and, periapical and panoramic radiographs. The oral radiologist showed the best performance among the various professionals. Through the analysis of images examinations, it could be affirmed that CT is more accurate than periapical and panoramic radiographs in diagnosing the dental etiology of MS. Despite the favorable outcome in relation to CT, the authors added that the diagnosis of odontogenic MS does not depend only on the type of image exam, but more specifically on the evaluator who will perform it Simuntis *et al.*, 2017. Due to the proximity of the roots of the upper teeth to the maxillary sinuses, once these teeth have infections, they can affect the maxillary sinuses. Among the studies included in the qualitative analysis of this systematic review, three evaluated which teeth were most affected by odontogenic MS. The most affected teeth were the upper first molars (31.6% -55%), the upper second molars (33.3% -50%) and the upper second premolars (8-12.8%), while the palatal root of the upper first molars was the root most associated with odontogenic MS (Maillet *et al.*, 2011; Mehra, Jeong, 2019; Simuntis *et al.*, 2017; Turfe *et al.*, 2019). Odontogenic causes are quite common in UMS. Despite this association, odontogenic etiologies are often overlooked by general practitioners and otorhinolaryngologists, since the odontogenic etiology may not be seen in radiographic examinations. It is suspected that there is a lack of knowledge on the part of professionals in relation to association of dental etiologies with MS. de Lima CO *et al.*, 2017 and Wang KL *et al.*, 2015 concluded that MS should be approached in a multidisciplinary manner and cite that the interaction between otolaryngologists and oral surgeons can be extremely beneficial to patients with suspicions of odontogenic MS.

CONCLUSION

The present systematic review showed a high prevalence of periapical diseases as the main etiology of MS. Most studies analyzed indicated endodontic factors as the most common cause, with a prevalence ranging from 18% to 94.9%. Thus, we emphasize the importance of

this fact for the endodontist, since the upper posterior teeth may have an intimate relationship with the maxillary sinuses. Once these teeth are affected by periapical disease, this type of disease can progress to MS. Misdiagnosis of an odontogenic etiology of MS can lead to inadequate treatment without solving the root cause of the problem.

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