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Presepsin assessment in maxillo-facial infections: a new early biomarker of sepsis?

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Abstract. Odontogenic infections can cause serious inflammatory problems of the soft and hard tissues in the maxillofacial area up to, albeit in quite remote circumstances, involvement of the brain tissues. In recent years, therefore, a holistic diagnostic-therapeutic approach has been developed in the management of odontogenic infections by carrying out a careful systemic history of the patient who has an infectious condition in the oral cavity. The early detection of systemic sepsis conditions was facilitated using serum biomarkers such as PCR, Procalcitonin (PCT) and Presepsin (PSEP) in hospital emergency rooms. However, even if used in combination, their diagnostic accuracy is such as to suggest the importance of researching new, more specific, and sensitive biomarkers. A total of 9 articles was analyzed to investigate the use of the PSEP as biomarker in the maxillo-facial region infections and including only English-language articles and the electronic search of publications from 1 January 2017 to 31 December 2021. This study aimed to determine the diagnostic value of presepsin in condition of sepsis derived from an odontogenic infection and to evaluate its use in the prognostic evaluation phase of surgical interventions performed in the maxillofacial area.

Keywords: sepsis, dentistry, presepsin, odontology infection.

INTRODUCTION

Odontogenic infection is a type of bacterial infection that can appear in the maxillofacial region (1). When it is affected by the fascial spaces it can cause cavernous sinus thrombosis and sepsis, including facial and cervical necrotizing fasciitis (2). Sepsis (S) can lead to systemic tissue damage, organ failure, and death. Therefore, early S diagnosis can have a significant impact on patient's management and prognosis. On this scenario the assessment in biological fluids of new biomarkers of S can be useful to determine the severity of the patient's inflammatory and infectious conditions (3). More recently, presepsin (PSEP) as an early biomarker of S in adults, pediatric and infant patients has been proposed (4,5).

Table 1. Risk associated with anatomical location.

Risk	Low	Moderate	High	Extreme
Spaces	Vestibular	Submandibular	Lateral pharyngeal	Mediastinum
	Infraorbital	Submental	Retropharyngeal	
	Buccal	Sublingual	Pretracheal	
		Pterygomandibular		
		Submasseteric		
		Temporal		

PSEP or soluble CD14 subtype (sCD14-ST) is a 13kDa fragment derived from the cleavage of CD14, a cell surface antigen cluster marker protein expressed in bone marrow anchored to the membrane of monocytes, macrophages, and polymorphic neutrophils (6,7). CD14 acts as a receptor for lipopolysaccharides complexes (LPS) and for the specific binding protein of LPS (LBP); it can bind to peptidoglycans and other surface structures present in both Gram-Positive and Gram-Negative bacteria. Once bound, the LPS-LBP complex activates the intracellular inflammatory response of the Toll-Like 4 receptor (TLR4) initiating the host inflammatory cascade against the infectious pathogen; phagocytosis and plasma protease activity result in the formation of the sCD14 subtype fragment (8,9).

The immune response occurs when various pathogen-associated molecular patterns are into contact with the pathogen, where sCD14 acts as a ubiquitous coreceptor, but sCD14 itself is not a specific factor for sepsis caused by bacterial infection. However, it has been shown that PSEP levels, unlike other inflammatory biomarkers, increase very rapidly (2-4 h) in the presence of systemic infections in adults, children, and newborns, thus determining diagnostic speed and therapeutic possibilities (10,11).

In accordance with previous findings, PSEP has been shown to play a key role in the diagnosis of sepsis caused by various organ infections (12).

The purpose of the present mini review was to offer an update on the potential role of PSEP as an early biomarker of S in patients requiring maxilla facial surgery and/or odontostomathologic care (13,14).

MATERIALS AND METHODS

This mini-review was performed in accordance with the PRISMA (Systematic Reviews and Meta-analyses) statement as shown in Figure 1. Extensive research on the literature and papers related to PSEP used as a diagnostic marker in maxilla-facial infections was performed

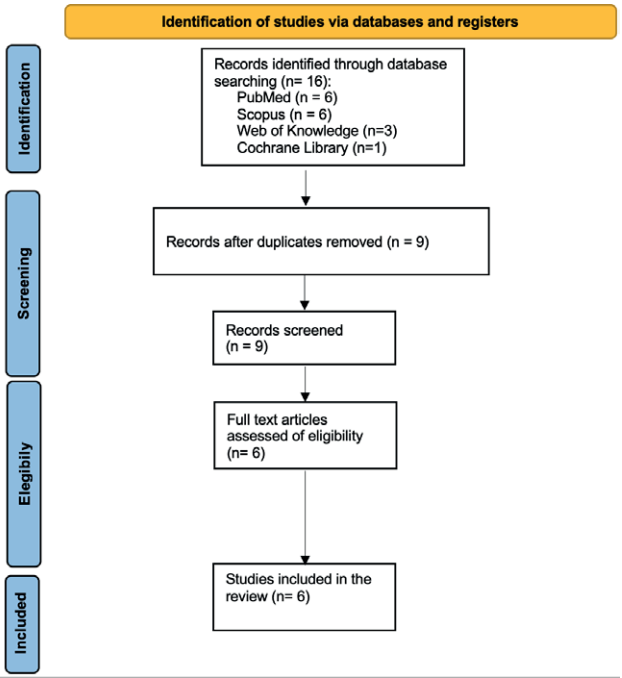

Figure 1. research method used to identify studies to be included in the review.

on the databases of PubMed (Medline), Scopus, Web of Knowledge, and Cochrane Library. Preferred Reporting Items for the research was performed by using combinations of the following keywords: "sepsis " AND "dentistry" OR "presepsin ". The search included only English-language articles and the electronic search of publications from 1 January 2017 to 31 December 2021 was conducted. The search strategy

used a combination of free-text words. To exclude duplicates, the references of the identified records were uploaded as Research Information Systems files into Zotero (RRCHNM, Fairfax, Virginia).

RESULTS

The search strategy reported records, including duplicates: **6** from PubMed, **6** from Scopus, **3** from Web of Knowledge, **1** from Cochrane Library**.** The duplicates were eliminated, thus all the selected databases produced **9** records. Data obtained are the result related to the use of PSEP as a diagnostic marker in the maxillo-facial infections.

DISCUSSION

Odontogenic infections, the most common cause of bacterial infections in the maxillofacial region, rarely progress to sepsis. However, the possibility of progression to sepsis cannot be excluded in cases of moderate or severe infections affected by the fascial spaces (15). According to Kang et al, PSEP can also be useful in determining the severity of odontogenic infection and sepsis, and when combined with existing test methods, it is expected to be better in evaluating patient prognosis. In fact, according to this study, a PSEP level of 671.5 pg/ml or higher for odontogenic infection can be considered an abnormal level (16).

Odontogenic infections can induce the condition of sepsis, caused by the abnormal response of the immune system of our body due to the onset of tissue damage that compromises the functionality of the organs and can lead to death. Furthermore, the COVID-19 pandemic has imposed new difficulties and challenges; for example, the use of tele-dentistry, thus modifying the dental practitioner / patient relationship. Therefore, it would be useful, in dental practice, to introduce the use of markers that can assess the actual risk of sepsis during surgical dental procedures. Several clinical parameters have been used as prognostic indicators for the severity of the infection. C-reactive protein (CRP), Procalcitonin (PCT), fever and anatomical locations have been investigated for the assessment of the extent of odontogenic infections (17). Recently, PSEP was identified as a marker of sepsis, in fact, based on the data collected previously, the sensitivity and specificity of PSEP were 78.95% and 70.83%, respectively. It is reasonable to think that further studies should investigate the use of PSEP as an earlier diagnostic marker of dental infections and as a prognostic tool in the healing processes of oral tissues after surgery, analyzing its concentration not only in serum, but also in other fluids oral such as saliva to reduce the emotional stress of the patients who must undergo the sampling (18).

CONCLUSIONS

Persistent odontogenic infections can be a common cause of sepsis in the head and neck. Infection frequently spreads in a predictable pattern within the fascial spaces of the neck and can result in airway compromise.

The focus of infection was mandibular in 70.1% and maxillary in 29.9%. Further findings regarding biomarkers, including PSEP, would be desirable in the diagnosis of this condition and in the prognosis of oral inflammatory diseases, such as periodontal disease, which can lead to systemic impairment (19,20)

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