RESEARCH REPORTS
Clinical

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Quality Difference in Craniofacial Pain of Cardiac *vs.* Dental Origin

ABSTRACT

Craniofacial pain, whether odontogenic or caused by cardiac ischemia, is commonly referred to the same locations, posing a diagnostic challenge. We hypothesized that the validity of pain characteristics would be high in assessment of differential diagnosis. Pain quality, intensity, and gender characteristics were assessed for referred craniofacial pain from dental (n = 359) *vs*. cardiac (n = 115) origin. The pain descriptors "pressure" and "burning" were statistically associated with pain from cardiac origin, while "throbbing" and "aching" indicated an odontogenic cause. No gender differences were found. These data should now be added to those craniofacial pain characteristics already known to point to acute cardiac disease rather than dental pathology, *i.e.,* pain provocation/aggravation by physical activity, pain relief at rest, and bilateralism. To initiate prompt and appropriate treatment, dental and medical clinicians as well as the public should be alert to those clinical characteristics of craniofacial pain of cardiac origin.

KEY WORDS: acute myocardial infarction, cardiac ischemia, craniofacial pain, dental pain, and referred pain.

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INTRODUCTION

Approximately 1% of medical emergencies in dental practice result in patient death and are mostly associated with acute cardiac failure (Atherton *et al*., 1999). The estimated risk for British dentists encountering a patient death sometime during a 40-year career is between 1:12 and 1:19 (Atherton *et al*., 1999). A significant number of patients with atypical symptoms of acute coronary disease die as a result of missed diagnosis and treatment delay (McCarthy *et al*., 1993; Pope *et al*., 2000). Until recently, craniofacial pain constituting the sole symptom of cardiac ischemia has been poorly recognized (Kreiner *et al*., 2007). Early treatment of acute coronary disease plays a critical role in saving a patient's life. Accordingly, reperfusion therapy within the early phase of an acute myocardial infarction has been shown to significantly reduce the in-hospital mortality of patients (Kalla *et al*., 2006), and each 30-minute delay is associated with an increased relative risk of one-year mortality (De Luca *et al*., 2004).

There is medical concern because women who experience an acute myocardial infarction tend to receive appropriate therapy less often than men and have poorer outcomes (Cohen *et al*., 2005). Inadequate understanding of the difference in symptomatology between women and men during cardiac ischemia is likely to play an important role in the medical management disparities between genders (D'Antono *et al*., 2006). Women more often than men present with atypical symptoms of cardiac ischemia (Philpott *et al*., 2001; Patel *et al*., 2004; Chen *et al*., 2005). Concordantly, we found a significant female preponderance in our recent prospective study, which revealed that nearly 40% of consecutive patients experienced craniofacial pain during an acute ischemic event (Kreiner *et al*., 2007).

One of the main predisposing factors for a delayed or missed acute myocardial infarction diagnosis is the absence of chest pain (Chan *et al*., 1998). We recently revealed that, in the absence of chest pain during cardiac ischemia, craniofacial pain, not left arm pain, is the most prevalent pain location (Kreiner *et al*., 2007).

Whether referred craniofacial pain is induced by cardiac ischemia or by primary dental pathology, the areas of pain distribution coincide (Falace *et al*., 1996; Kreiner *et al*., 2007). Patients with craniofacial pain as the only symptom of cardiac ischemia are therefore likely to seek dental or otorhinolaryngological treatment. When the sole symptom of cardiac ischemia is pain in the teeth, temporomandibular joints, or other craniofacial structures, clinicians face a diagnostic challenge (Batchelder *et al*., 1987; Rothwell, 1993; Kreiner and Okeson,

1999). Our objective was to delineate any differences in clinical presentation of pain due to cardiac *vs*. dental origin, with the aim of providing clinicians with better clinical criteria for early differential diagnosis. We hypothesized that the quality of referred craniofacial pain from dental origin would have a neurovascular "throbbing" quality unlike referred cardiac pain. We further expected the diagnostic validity for pain intensity to be low.

MATERIALS & METHODS

Study Populations

Patients with Craniofacial Pain Referred from Cardiac Origin

Patients with a verified cardiac ischemic episode and pain referral to the craniofacial structures were derived from a total of 348 individuals (145 females, 203 males) ranging in age from 41 to 88 yrs, with a mean age of 65 yrs, who were admitted with signs and/or symptoms suggesting cardiac ischemia to three cardiology units in Montevideo, Uruguay. Patients were seen consecutively during one-month recruitment periods that took place in 2001, 2002, 2004, 2007, and 2008. Periods were spread over the year to avoid seasonal effects.

Cardiac ischemia and acute myocardial infarction were diagnosed by cardiologists according to the American College of Cardiology definition (Cannon *et al*., 2001). Patients were excluded if cardiac ischemia was not verified or if they had no craniofacial pain referral, asymptomatic ischemia, craniofacial pain of non-cardiac origin or could not communicate appropriately. We excluded 233 patients who had normal cardiologic evaluation (n = 24), asymptomatic ischemia (n = 9), severe heart failure (n = 3), psychiatric disorders and confusion (n = 2), pain from non-cardiac origin (n = 15), and no craniofacial pain referral from cardiac origin (n = 180). A group of 115 patients (56 females, 59 males, mean age 64 yrs) met the inclusion criteria and comprised the study population. Calibrated investigators conducted the examinations (Kappa = 0.908).

Patients with Craniofacial Pain Referred from Dental Origin

Patients with craniofacial pain referred from dental origin were derived from a total of 400 patients (217 females, 183 males, age range 17 to 73 yrs) reporting to the dental emergency clinic at the University of Kentucky, College of Dentistry, Lexington, USA (Falace *et al*., 1996) with complaint of posterior toothache. The inclusion criterion was posterior toothache clinically verified as being attributed to one tooth according to acknowledged criteria (Cailleteau, 1995). The study group (dental craniofacial pain group) was comprised of 359 patients (196 females, 163 males) with dental pain that referred to the craniofacial region. Seventeen patients were unable to rank pain intensity and were excluded from intensity analysis. One of the authors conducted all examinations.

Sample size calculations were performed with the Kelsey and Fleiss formula, assuming a power of 80% and accepting a statistical difference at the 5% level. A minimum sample size of 98 individuals was needed for the cardiac craniofacial pain group and 245 for the dental craniofacial pain group.

Methods

Demographic details and health history were assessed. Patients were asked to describe the quality of their pain using the list of pain descriptors from the McGill Pain Questionnaire (Melzack, 1975), which is psychometrically validated for both English and Spanish (Melzack, 1975; Lázaro *et al.,* 2001), and also with their own words. They were asked to describe the pain using as many descriptors as needed. Pain intensity was marked on a numerical rating scale ranging from 0 to 10, which has been validated for corresponding verbal descriptors (Borg, 1982) as follows: 0, "Nothing at all"; 1, "Very weak"; 2, "Weak"; 3, "Moderate"; 4, "Somewhat strong"; 5-6, "Strong"; 7-8-9, "Very strong"; and 10, "Extremely strong". Painful areas were marked on a full-body schematic drawing with views of the intra-oral, head, and neck areas.

Considering the non-Gaussian distribution of the samples, we used non-parametric tests to compare pain intensity (Mann Whitney & Wilcoxon) and quality (Chi-square) between groups and genders using SSPI software (Version 9, Chicago, IL, USA). We used the "epiR" and "stats" packages of the "R" software program to perform a discriminative analysis to evaluate the diagnostic potential of the findings (sensitivity, specificity, etc.) and to make ROC curves. Control for co-variables was performed with a logistic regression model. We used the Wilcoxon Signed Ranks Test for paired samples to analyze the intra-individual differences for pain intensity.

Ethical Approval

The Ethics Committees at the Universidad de la República and the Hospital Central de las Fuerzas Armadas, Uruguay, and the University of Kentucky, USA, approved the pertinent section of the study protocol. Informed consent was obtained from each included patient.

RESULTS

Pain Quality

When patients with cardiac ischemia felt pain in multiple areas of the body, the pain was consistently (100%) described to be of the same quality between intra-individual sites.

Dental Craniofacial Pain *vs.* Cardiac Craniofacial Pain

There was no statistically significant difference in gender distributions between the dental and cardiac craniofacial pain groups ($p = 0.53$). Four quality descriptors (aching, burning, pressure, and throbbing) were found to have high validity for guiding to a differential diagnosis (Table). The descriptor "sharp" was used by both groups, with a preponderance in the dental group ($p < 0.001$). Overall distribution of pain quality descriptors differed between groups (Fig.).

There was no gender difference regarding pain quality in either group. After most data of the dental craniofacial pain group were statistically analyzed, the corresponding questionnaires with demographic data were destroyed by an accident and the mean age calculations lost. However, we know that the mean age was around 35 yrs.

Table. Discriminative Analysis for Those Quality Descriptors with High Clinical Relevance (CI, confidence interval; CFP, craniofacial pain)

Descriptor	Positive Dental CFP Group	Positive Cardiac CFP Group	Specificity with 95% CI	Sensitivity with 95% CI
Aching	n = 215	n = 5	0.96 (0.91, 0.98)	0.6 (0.55, 0.65)
Burning	n = 22	n = 54	0.94 (0.91, 0.96)	0.47 (0.38, 0.56)
Pressure	n = 0	n = 78	1 (0.99, 1)	0.68 (0.59, 0.76)
Throbbing	n = 211	n = 1	0.99 (0.96, 1)	0.59 (0.54, 0.64)

We estimated the statistical power of detecting a difference for respective quality descriptors between the dental and cardiac craniofacial pain groups by applying a normal approximation with continuity correction. Based on the available sample sizes, our study had almost 100% power to detect the observed differences for "pressure", "burning", "aching", and "throbbing".

Craniofacial Pain as the Sole Symptom during Cardiac Ischemia

Eighteen patients (6%) reported craniofacial pain as the sole symptom of cardiac ischemia. The descriptors "pressure" and/or "burning" were used by all except one patient in this group, with "pressure" being more frequently reported by those patients without acute myocardial infarction (p = 0.017).

Pain Intensity

There was no gender difference regarding pain intensity. Pain intensity was higher in the dental craniofacial pain group than in the cardiac craniofacial pain group (p = 0.043). Most patients in both groups (> 77%) rated their pain intensity as strong or worse. ROC curve analysis for intensity showed an area under the curve of 0.583 (95% CI = 0.52-0.64).

An intra-individual comparison within the cardiac craniofacial pain group revealed pain in the craniofacial regions to be significantly less intense than pain in typical anginal areas (p = 0.001), with no difference by age or gender.

DISCUSSION

The quality of pain referred to the same craniofacial regions was found to differ significantly between pain of cardiac origin and pain of dental origin and with no difference between genders.

The quality descriptors with the strongest association with craniofacial pain of cardiac origin were "pressure" and "burning". "Pressure" was used by two-thirds of patients in the cardiac craniofacial pain group, but none in the dental craniofacial pain group. The absence of pressure-like pain in the dental craniofacial pain group is consistent with the results of experimentally induced dental pain (Ahlquist and Franzén, 1994; Ikeda and Suda, 2003). The use of the descriptor "suffocating" indicated a cardiac origin, because only patients in the cardiac craniofacial pain group used it, but the limited sample size using "suffocating" to describe their pain yielded a power slightly below 80%.

The pain descriptors pointing to a dental origin were "throbbing" and "aching", each of them used alone or in combination by almost two-thirds of patients in the dental craniofacial pain

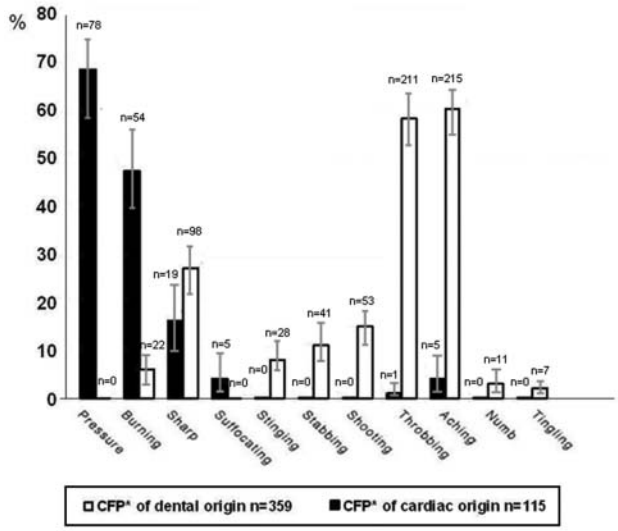

Figure. Distribution of quality descriptors for craniofacial pain referred from cardiac and dental origins. Error bars represent 95% confidence intervals. * CFP = craniofacial pain.

group. Only one patient in the cardiac craniofacial pain group used the descriptor "throbbing". However, it seems that the perception of the quality of pain of cardiac origin can vary with different physiological and experimental conditions. Hence, "throbbing" and "numbness" in the head and neck have been reported by 15% of patients who experienced chest pain associated with cardiac ischemia during exercise stress-testing (D'Antono *et al*., 2006). It seems likely that the experimental setting of exercise stress-testing may precipitate a neurovascular throbbing component as well as a numb sensation in the craniofacial structures that are not usually reported by patients during non-experimental conditions. This hypothesis is given further support by the finding that women reported chest pain more often than men during daily activities, but not during exercise (Sheps *et al*., 2001).

Cardiac ischemia is diagnosed primarily in middle-aged and elderly patients, while dental pain frequently occurs also in younger adults and adolescents (Pau *et al*., 2007; Teoh *et al*., 2007; Bastos *et al*., 2008). Hence, the age range of our patient samples is in accordance with the general population. It is reasonable to regard the missing age data in the dental craniofacial pain group as having little impact on the results of this study, because age does not influence the quality of dental pain (Ikeda and Suda, 2003).

Pain intensity was significantly higher in patients with craniofacial pain from dental origin, but the ROC curve analysis showed

that intensity had a poor accuracy to differentiate between pains from cardiac *vs*. dental origin. While pain quality was consistent between different intra-individual locations, the pain intensity was significantly more intense adjacent to the cardiac source. The mechanisms underlying these differences in quality and intensity perception patterns are probably related to the complexity of the brain-processing of cardiac pain. The secondary somatosensory (SII) cortex and the posterior insula cortex are involved in the intensity encoding of visceral pain, and many bilateral networks of cortical structures are involved in the processing of other pain dimensions (Dunckley *et al*., 2005). Also, the convergence of visceral and somatic inputs onto common circuits in the central nervous system, including the trigeminal nucleus (Sessle *et al*., 1986; McMahon, 1997; Chandler *et al*., 1999) and the central sensitization phenomenon (Giamberardino *et al*., 1997; Laird *et al*., 2001), may be involved in the clinical findings of this study.

The two patient groups were recruited in cities from different countries, Lexington, KY (USA) and Montevideo, Uruguay (South America), respectively. Because the McGill questionnaire is validated for both English and Spanish, and gender distributions agreed between groups, the highly significant differences in pain quality reported for craniofacial pain of cardiac *vs*. dental origin should not be biased.

Study limitations were mostly related to the small sample size of the subgroup of patients with craniofacial pain as the sole symptom of cardiac ischemia. Future studies are planned for more detailed analysis of this group of patients. The accidental loss of individual data for the dental group made it impossible to control for some co-variables. As discussed in a previous paragraph, this is not anticipated to have a significant impact on the results or in the interpretation of the findings.

Since almost 80% of patients with craniofacial pain as the sole manifestation of cardiac ischemia described their pain as strong or worse, it can be assumed that many of these patients may seek dental rather than medical treatment. To initiate prompt and appropriate treatment, dental and medical clinicians as well as the public should be alert to those clinical characteristics of craniofacial pain that make a cardiac origin more likely than a dental origin.

Characteristics known to indicate acute cardiac disease rather than dental pathology as the origin of craniofacial pain include: pain provoked/aggravated by physical activity, pain relieved by rest, and bilateralism (Kreiner *et al*., 2007). In a real clinical setting, the clinician has to differentiate between many types of referred pain to the craniofacial region. While the pain descriptors did not show simultaneous high values of sensitivity and specificity, the high specificity values point to the diagnostic relevance of the findings. In conclusion, differential diagnosis can now be improved by the knowledge that "pressure" and/or "burning" pain strongly indicates acute cardiac disease. In the cases of craniofacial pain from suspected cardiac origin, the patient should be sent to the hospital for urgent cardiologic evaluation.

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