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Comparison of planar bone scintigraphy and single photon emission computed tomography for diagnosis of active condylar hyperplasia

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ABSTRACT

Purpose: The aim of this study was to compare the reliability and correlations with age and gender of two nuclear medicine tests used for diagnosis of active condylar hyperplasia, namely, planar bone scintigraphy versus single photon emission computed tomography (SPECT).

Material and method: This was a descriptive observational study carried out in 61 patients (38 women and 23 men) clinically diagnosed as having facial asymmetry and suspected unilateral condylar hyperplasia. The patients had both planar bone scintigraphy and SPECT diagnostic imaging as well as reference data of the percentage of $^{99}Tc^{m}$ MDP (methylenediphosphonate) uptake in the condyle, clivus, and fourth lumbar vertebra (L4), respectively, for SPECT and planar scintigraphy calculations. Radioactive counts were measured per region of interest and the respective ratios were calculated. The age range of the patients was 13–50 years (mean ± standard deviation = 21.16 ± 8.75). The two groups were compared by a nonparametric (Mann–Whitney *U* test. Uptake percentage and delta values had normal distribution and consequently were compared by a Student *t* test.

Results: A total of 61 anterior planar images and 61 SPECT images were compared. Eight patients presented high uptake in planar bone scintigraphy images (13.11%), while 32 patients (52.46%) had high uptake with SPECT. The prevalence of condylar hyperactivity was higher in women than in men both for right condyle (ratio 4:3) and for left condyle (10:1) and the prevalence was significantly higher for the right condyle.

Conclusion: The study indicates that SPECT is more sensitive to identify condylar hyperactivity as compared to planar bone scintigraphy in patients with clinical presumptive diagnostic of condylar hyperplasia.

1. Introduction

Condylar hyperplasia (CH) is a pathologic condition characterized by excessive growth of one condyle (rarely bilateral) that may cause asymmetric facial deformities and malocclusion. Although, it is self-limiting, it may be active when normal growth is completed. The progressive excessive growth of one condyle may compromise the neck, mandibular ramus, and body, and it causes symptoms of pain and articular dysfunction (Nitzan et al., 2008; Elbaz et al., 2014). It is most frequently found as active condition in 11- to 25-year-old patients, and then it may be present in passive form as clinical sequelae (Nitzan et al., 2008; Eslami et al., 2003). A higher prevalence in women than in men has been reported by Raijmakers et al. (2012). Its etiology has been related to genetic factors, trauma, tumors, or hormonal conditions (Obwegeser et al., 1986; Anaya, 2002).

The diagnostic clinical impression of CH is made from a combination of facial, intraoral, radiographic, or tomographic findings, but bone scintigraphy is the current gold standard to assess bone hyperactivity in condyles suspected to be associated with excessive cellular activity. The diagnostic is confirmed only by histopathology, when the patient is subject to surgical intervention.

According to age, esthetic compromise, severity of the malocclusion, and level of articular dysfunction, this pathology demands a thorough diagnostic workup using extraoral photography, study casts both static and articulated, panoramic and postero-anterior X-ray films, tomography with three-dimensional reconstruction, bone scans by planar gammagraphy and/or single-photon emission

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tomography (SPECT), and histopathology (López and Corral, 2015; Villanueva et al., 2011).

The early diagnostic of CH is important, as the treatment opportunity may reduce further structural damage; treatment protocols are different according to the patient's age, severity of the resulting asymmetry, and the active or passive status of the pathology (Munoz et al., 1999; Motamedi, 1996).

Usually, it is the orthodontist or the maxillofacial surgeon that performs the clinical diagnostic and orders bone scintigraphy studies to evaluate the active or inactive status of the disease.

SPECT imaging is obtained from radioactive counts emitted after tissue absorption of the radioactive isotope technetium 99 metastable, bonded to methylendiphosphonate (MDP) ($^{99}Tc^{m}$-MDP). SPECT is commonly used to evaluate the metabolic activity in several types of tissue, and it is considered to provide functional and morphological information about the tissue (Saridin et al., 2007 Saridin et al., 2011 Pogrel et al., 1995).

Gammagraphy is the production of two-dimensional images of the distribution of radioactivity in tissues after the internal administration of a radio-pharmaceutical agent, obtained by a scintillation camera. Planar bone scintigraphy is a gammagraphic scanning imaging modality that differs from SPECT, as the reference to compare condylar uptake is often the fourth lumbar vertebra, whereas in SPECT the reference is clivus uptake. Both techniques are considered sensitive but poorly specific (Chan et al., 2000; Wen et al., 2014; Saridin et al., 2008). Therefore, the results should be interpreted in connection with clinical findings to achieve accurate diagnosis and to plan the ideal treatment so as to avoid the development of further severe facial asymmetries and malocclusion and to provide a better prognosis (Sora and Carolina, 2005; Wolford et al., 2014).

The objective of the present study was to compare two methods of nuclear medicine imaging (planar bone gammagraphy vs SPECT) performed in patients with facial asymmetry, and to explore correlations with patient characteristics.

2. Material and methods

2.1. Patients and protocol

This study protocol (number 017-012) was approved by the Ethics Committee of the Universidad del Valle (Cali, Colombia). The study conformed to the principles of the Declaration of Helsinki, and all patients signed informed consent forms before any intervention.

The study included 61 patients, 10–50 years old, that had been send to the nuclear medicine center (Gamanuclear, Cali, Colombia) because they had a preliminary clinical diagnosis of facial asymmetry and clinically suspected CH. All patients underwent planar gammagraphy and SPECT scans. Patients with antecedents of condylar tumor, mandibular trauma, previous condylar surgery, arthritis, or autoimmune disease were excluded.

The gammagraphic scans were obtained with high-resolution, low-energy collimators 3 h after the administration of a diagnostic dose of $^{99}Tc^{m}$ MDP (20 mCi) by intravenous injection. The static lateral skull image was obtained with a matrix of 256×256, and 700,000 counts per projection. The cranial tomographic images were obtained using a matrix of 64×64, 360° of rotation at 15 s per frame.

The processing of planar images was performed by inspection of regions of interest (ROIs) drawn around each condyle and around the L4 vertebra. For SPECT, a transaxial frame was obtained to visualize condyles and clivus, structures of reference, along the same axis. For additional view analysis of the tomographic images, coronal and sagittal images were used.

All of the registered data were generated by the computer system SEGAMI (Segami Corporation) and software MIRAGE, previously calibrated, without any direct operator generating data from the images.

Quantitative results from both planar gammagraphy and SPECT were gathered from left and right condyle in the preselected ROI (Figs. 1 and 2), calculating the ratio of uptake by the following formula:

$$\text{Condyle \% uptake} = \frac{\text{condyle counts}}{\text{Left counts} + \text{right counts}} \times 100$$

A percentage of condylar uptake 55% or higher, generating differences of 10% or more (Delta value) between condyles was registered as indicative of active unilateral condylar hyperactivity (AUCH).

The ratio or relative uptake was determined from the radioactive counts per condyle and counts for clivus in the case of SPECT, and for L4 in planar gammagraphy, taking into account the background radioactive counts (Fig. 3), using the following formula:

$$\text{SPECT ratio} = \text{Counts per region} - \text{background counts} \\ /\text{Clivus counts} - \text{background counts}$$

$$\text{PLANAR ratio} = \text{Counts per region} - \text{background counts} \\ /\text{L4 counts} - \text{background counts}$$

2.2. Statistical analysis

Demographic variables and results are expressed as mean and standard deviation. The distribution of gammagraphic data was not normal (Shapiro–Wilk test); therefore the two groups were compared by a nonparametric test (Mann–Whitney *U*). Uptake percentage and delta values had normal distribution and

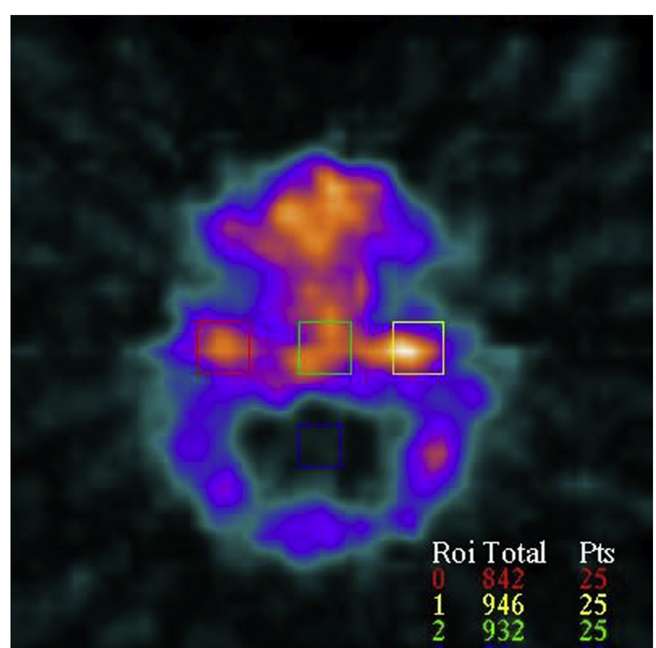

Fig. 1. Regions of interest selected in coronal section for SPECT, and counts. In this figure, 0 is the right condyle 1 is the left condyle, 2 is clivus, and 3 is the background count.

Fig. 2. Regions of interest in coronal section for PLANAR and right and left condyle counts.

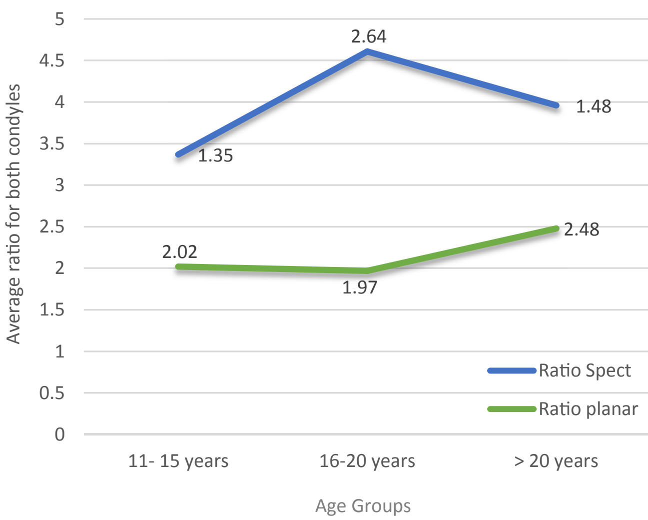

Fig. 3. Average ratio for both condyles, per groups of age, and techniques.

consequently were compared by a Student *t* test. The percentage of agreement in the diagnostic by the two techniques was expressed by the kappa coefficient, which is considered acceptable if the percentage of agreement is >75%. As kappa values were very low, the corresponding *z* values was not calculated. The coefficient of Stewart–Maxwell for condylar status (normal, increased, or reduced) was not applicable because of the very low percentage of agreement.

3. Results

The sample of 61 patients included 38 women (62.3%) and 23 men (37.7%). The range of age was 13–50 years, and the general mean ± standard deviation was 21.16 ± 8.75 years (for women it was 22.02 ± 9.39 years and for men 19.73 ± 7.55 years). Although, the 61 patients had a presumptive clinical diagnostic of CH, eight (13.11%) were condyle hyperactive cases according to planar bone scintigraphy and 32 (52.46%) according to SPECT (Table 1).

The level of condylar uptake according to age was different for SPECT as compared to planar results. The youngest patient with high uptake by planar technique was 16 years old, whereas with SPECT the youngest was 13 years old. The oldest patient with high uptake by Planar technique was 23 years old, whereas with SPECT the oldest patient was 45 years old.

The ratio or relative uptake per groups of age was different for each technique, as shown in Table 2.

There was no linear correlation between ratio and age as some authors have suggested (Nitzan et al., 2008; Villanueva et al., 2011; Cisneros and Kaban, 1984). The same lack of correlation is conclusive when the interquartile values are compared for hyper-uptake and normal-uptake patients. For instance, the values for the median (Q2) obtained with SPECT in the high-uptake group were 1.22 for the 11- to 15-year-old group; 1.16 for the 16- to 20-year-old group; and 1.04 for the >20-year-old group. For normal-uptake patients, the corresponding values were 0.99/1.21/0.56. In both examples, there was no linear correlation with age (Table 3).

In general, there was no agreement<<? between results of the diagnostic techniques ($p > 0.19$) except for the delta value of the difference between right and left condyles, which had an acceptable kappa coefficient.

4. Discussion

It is broadly accepted that the diagnostic of CH should be based on a thorough facial and intraoral clinical examination of the

Table 2
Ratio (average ± standard deviation [SD]) of study groups, by age and technique<<?

Average ratio ± SD for both condyles			
Age group, y	n	Ratio (planar)	Ratio (SPECT)
11–15	17	2.02 ± 1	1.35 ± 0.86
16–20	21	1.97 ± 1	2.64 ± 4
>20	23	2.48 ± 1.84	1.48 ± 1.67

Table 3
Interquartile values (Q) for hyper-uptake and normal-uptake subjects.

Technique and age group	Hyper-uptake (n = 8)			Normal-uptake (n = 53)		
	Q1	Q2	Q3	Q1	Q2	Q3
Planar						
11–15 y	—	—	—	1.15	1.8	2.72
16–20 y	0.82	1.6	1.91	1.12	2.02	2.66
>20 y	2.23	2.23	2.23	1.11	1.79	3.67
	Hyper-uptake (n = 32)			Normal-uptake (n = 29)		
SPECT						
11–15 y	0.95	1.22	1.36	0.94	0.99	1.88
16–20 y	1.06	1.16	2.29	0.6	1.21	2.02
>20 y	0.78	1.04	2.2	0.32	0.56	0.96

Table 1
Frequency of cases of high uptake (>55%) in right and left condyles (C), by gender and technique.

	Women (n = 38)		Men (n = 23)		Total (n = 61)
	Right C	Left C	Right C	Left C	
	n (%)	n (%)	N (%)	n (%)	n (%)
Planar	3 (7.89)	1 (2.63)	2 (8.70)	2 (8.70)	8 (13.11)
SPECT	12 (31.58)	10 (26.32)	9 (39.13)	1 (4.35)	32 (52.46)

patient, as well as on radiographic and/or tomographic images, as indicated by others (Kubota et al., 1999; Bishara et al., 1994; Grummons et al., 1987). However, it is also very important to establish the active or passive stage of the hyperplasia, which is possible by bone scintigraphy at the condylar level (Wen et al., 2014; Cisneros et al., 1984; Olate et al., 2013). The methods of nuclear medicine allow the identification of bone growth centers in the condylar region (Henderson et al., 1990; Fahey et al., 2010), and their<<? VS ITS<<? clinical relevance has been discussed by Hodder et al. (2000) and Olate et al. (2013). Early diagnosis of CH may help to prevent the development of severe asymmetries and deformations in the three space planes with its esthetic, functional, and psychological sequelae.

According to many studies and the systematic review by Raijmakers et al. (2012), CH is significantly more prevalent in women than in men, and this tendency is so clear that this author suggests that female gender should be considered a risk factor for UCH.<<? BEGIN The whole sample in this study included more women than men, indicating that in the Colombian population, there are also more cases detected in women, although it could be that women more frequently attend clinics seeking esthetic facial treatments. In any case, SPECT detected 22 positive cases of CH in women and 10 in men.

The highest prevalence of UCH and other temporomandibular joint (TMJ) disorders is associated with hormonal differences, particularly those related to estrogens that participate as bone growth regulators. Estrogen receptors are present in articular cartilage and in growth plates, and there is experimental evidence of local synthesis of estrogens in the TMJ, as reported by Talwer et al. (2006), Abubaker et al. (1993).

This study provides further evidence that the SPECT technique is more sensitive than planar scanning for detecting abnormal condylar uptake (52.46% cases vs 13.11%, $p < 0.0001$). This result is coincident with all of the previous studies that compare the two techniques; for instance, Wen et al. (2014) reported 95% sensitivity and 62.1% specificity for the SPECT technique. A previous meta-analysis published by Saridin et al. (2011) calculated a sensitivity of 0.90 for SPECT and 0.71 for planar bone scans and a specificity of 0.95 for SPECT and 0.92 for planar scans. Although, the difference in sensitivity is statistically significant, the specificity is not significantly different between the two techniques. In the present study, it was not possible to calculate specificity, as the subjects were not surgically treated and, as a result, we had no histopathology. A false-positive result, with either SPECT or planar scan, may be produced by any increase in bone metabolism or vascularization in the condylar area due to infection, inflammatory disease, trauma, neoplasia, or hyperplasia (Pogrel et al., 1995). Specificity is the ability of the technique to distinguish actual negative cases (sound growth) from real pathologic conditions. In general, it is expected that there will be a lower specificity when the sensitivity is higher. The prevalence of UCH in the group studied calculated from SPECT data is significantly higher than that calculated by planar results because of the difference in sensitivity of the techniques. However, in general it is well known that radioisotope techniques are highly sensitive but that their specificity is limited, and therefore the results must be interpreted taking into account the whole clinical context.

Another aspect of discussion in the literature has been the correlation of scintigraphic data for the percentage of uptake or ratio with age. A study by Cisneros and Kaban (1984) indicated a perfect correlation with age, but in a very small number of cases per age group and using techniques now outdated. In the present study, we expected, using different statistical approaches, to detect this correlation with age, but the results indicate that such a correlation was not significant, either in subjects with normal uptake or in those with high uptake in any condyle.

Correlation between the results of one technique and the other in the present study ($r = 0.439$, $p < 0.01$) is higher than the value reported by Pogrel et al. (1995), who found a significant correlation between the two techniques ($p = 0.039$) as well.

No studies were found in the literature that inform the reader about changes in sensitivity and specificity related to different cut-off values (that is, the so called relative operation<<? RECEIVER OPERATING?<<? characteristics of SPECT). In this study, the usual cut-off point of 55% was taken as indicative of CH, as has been reported in the literature by Hodder et al. (2000). This cut-off could be more specific and better related to clinical findings and symptoms.

5. Conclusions

The present study indicates that SPECT is a bone scintigraphy technique more sensitive to identify hyperactive condylar tissue, as compared to planar gammagraphy. Using any of the techniques, an uptake value greater than 55% is suggestive of condylar hyperplasia; however, the diagnosis should be confirmed by a thorough clinical evaluation.

A higher prevalence of high condylar uptake of the radioisotope in women than in men was also confirmed. The right condyle was more often involved than in the left condyle.

No correlation between the ratio of uptake and age was confirmed for either of the two techniques compared.

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