



Self-reported participation restrictions in normal hearing individuals in thyroid ontogeny: Evidence of subclinical changes

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ABSTRACT

Purpose: To verify evidence of subclinical alterations through self-reported participation restrictions in normal hearing individuals and congenital hypothyroidism patients.

Methods: An analytical, quantitative, cross-sectional exploratory study with a 1:1 ratio, consisting of a convenience sample of 86 normal hearing individuals with (n = 42) and without (n = 44) congenital hypothyroidism diagnosis. All participants underwent tonal and speech audiometry, immittance and distortion product otoacoustic emissions. The researchers excluded people with hearing loss, genetic syndromes and metabolic diseases. The instrument used for evaluate of self-reported participation restrictions was the HHIE-adapted questionnaire, composed of 25 questions, 12 of which were social domain and 13 emotional domain. Student's t-test and chi-square test were used for statistical analysis at a significance level of 5%.

Results: There was a significant (p < 0.001) self-reported participation restrictions in CH (61.9%), with a greater relevance for the social domain (p = 0.002). There was a greater frequency of mild/moderate (40.5%) and higher prevalence of association with clinical factors and adherence to treatment.

Conclusion: The findings indicate that self-reported participation restrictions in normal hearing individuals with congenital hypothyroidism was more significant than in the non-exposed group, suggesting evidence of sub-clinical auditory abnormalities in this population.

1. Introduction

The close dependence of adequate levels of thyroid hormones for the normal development of the auditory system is already well discussed (Sohmer and Freeman, 1996; Sininger et al., 1997; Hashemipour et al., 2012), both in the pre- and postnatal moments, especially in the period known as critical for auditory maturation that begins at the end

of the first trimester of gestation and lasts until the first year of life (Sininger et al., 1997), which explains the association of hearing changes in congenital hypothyroidism (CH), even in cases with diagnosis and early treatment³.

Currently, with the early diagnosis and treatment of CH, hearing abnormalities do not coexist as frequently and severely as before the advent of Neonatal Screening Programs (NSP) (Rovet et al., 1996;

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Bellman et al., 1996). However, despite the evident improvements in the prognosis, these abnormalities may persist in a probable subclinical modality (Rocco et al., 2015), which is characterized by auditory alterations still in initial processes and the basic auditory evaluation may not detect, but can progress to the clinical form.

Thus, the existence of preclinical disorders in auditory pathways at early ages has the potential to disturb the adequate conduction of acoustic signals throughout the auditory system, causing linguistic, cognitive and/or socioemotional problems if not detected and treated.

Therefore, the importance of guidance, investigation and monitoring of the auditory health of individuals presenting factors that are harmful to the auditory system, such as CH, in order to prevent or minimize the deleterious effects arising from the probable injuries to the auditory pathways in this population.

Therefore, for a better understanding of hearing conditions in CH, a useful alternative may be the use of the auditory self-assessment questionnaire (Menegotto et al., 2011) as a screening method and complementary to auditory evaluation, since it presents high sensitivity, quick application and low cost (Rosalino and Rozenfeld, 2005).

In addition, these instruments provide the professional with a complete view of the functional auditory capacity (Weinstein and Katz, 1999), which contributes to the identification of the symptoms that precede a disturbance in the auditory system, even in the absence of a lowering of psychometric thresholds (Baruzzi et al., 2009). Thus, the hypothesis of this study is that in subclinical auditory abnormalities, normal hearing individuals with CH present self-reported participation restrictions (SRPR) to some degree.

Finally, the present study has as its primary objective to verify evidence of these alterations in this population through the evaluation of self-reported participation restrictions. As a secondary objective, to analyze the association of self-reported participation restrictions with clinical and laboratory aspects of thyroid ontogeny, as well as compare the findings with a normal hearing group without CH.

2. Material and methods

2.1. Study design

An analytical, quantitative, cross-sectional, exploratory study with a comparison group, with a sample obtained for convenience, approved by the Research Ethics Committee of the School of Nursing of the Federal University of Bahia, Opinion No. 534,704/2013. All participants were volunteers for the research, agreeing to participate by signing the Term of Free and Informed Consent by their parents or guardians, as well as signing the Term of Free and Clarified Assent whenever appropriate.

The researchers defined the following eligibility criteria for the composition of the exposed group sample: age ≥ 5 years; clinical diagnosis of confirmed CH according with the practical clinical guidelines for the management of hypothyroidism (Brenta et al., 2013); positive L-T₄ deprivation test after three years of age; not having other metabolic diseases, as well as any other form of hypothyroidism that is not congenital, is not suffering from syndromes, neurological or psychiatric diseases; absence of clinical history and risk indicators for auditory deficiency, auditory thresholds, for pure tone, of air conduction ≤ 25 dBHL and vocal within the normality standards confirmed in tonal and speech audiometry; presence of distortion product otoacoustic emissions at specific frequencies of 1–8 kHz in order to determine cochlear function at these specific frequencies; tympanometric curve of type A in the immittance audiometry.

The researchers adopted the same inclusion criteria for the non-exposed group, except for the need for a confirmed diagnosis of CH, discarded through the measurement of serum hormone levels in the Neonatal Screening Reference Service (NSRS).

2.2. Study population

The sample consisted of 86 participants divided into two groups:

Exposed group (EG): formed by 42 normal hearing patients, ranging in age from 5 to 15 years, all with confirmed diagnosis of CH and clinically characterized by a larger project entitled “Screening of mutations in genes implicated in thyroid ontogenesis in patients with congenital hypothyroidism.” All subjects were at least semi-illiterate and without prior knowledge of the self-reported participation restrictions assessment questionnaire. The researchers selected those who attended regularly for medical care at the NSRS.

Non-exposed group (NEG): composed of 44 individuals, relatives and/or acquaintances of NSRS users, with ages ranging from 5 to 15 years without diagnosis of CH or any other metabolic condition, confirmed by laboratory tests, normo-hearing and paired by socio-educational level, age group and sex in the proportion of 1:1. The sampling technique was non-probabilistic. These individuals were also at least semi-illiterate and had no prior contact with the questionnaire for the self-reported participation restrictions evaluation.

2.3. Collection procedures

Prior to the application of the questionnaires for the self-reported participation restrictions assessment, each participant underwent audiological evaluation. Patients with normal meatoscopy underwent tympanometry and stapedia reflex research with model AZ-7 (Interacoustics®, Drejervaenget, Denmark), ANSI S3.39-1987 calibration, TDH-29 handset, with a 226Hz probe tone to 70 dB. The researchers included individuals with tympanogram type “A” for analysis of otoacoustic emissions distortion product at the specific frequencies of 1–8 kHz, using the Vivosonic electrophysiological equipment, model Integrity V500 System, portable system and wireless technology (Amplitude®, Hannover, Germany) and in the performance of tonal and speech audiometry, clinical audiometer AD 229 (Interacoustics) and TDH-39 supraaural headphones (ANSI S3.6/96: ANSI S343/92; ISSO 389/91 calibration).

Consequently, the researchers investigated the frequencies of 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz, at a presumably audible intensity, around 25dBHL. They considered thresholds within the normality patterns of audiograms with airway values ≤ 25 dBHL and bone ≤ 15 dBHL (Silman and Silverman, 1997). In the possibility of a probable hearing loss, they classified the audiometric alteration according to type (Silman and Silverman, 1997) and degree (Lloyd and Kaplan, 1978), but they only considered the cases within normality standards in this study.

Therefore, the researchers used the instrument (Portuguese version) to evaluate self-reported participation restrictions, adapted for normal hearing individuals (Fernandes et al., 2014), from the HHIE questionnaire, Hearing Handicap Inventory for the Elderly.

The original HHIE version, written in the English language and adapted for the Portuguese language, is composed of 25 simple questions that quantify 13 items of emotional domain and 12 items of social/situational domain. Participation consists of marking a question by common item “X” corresponding to “yes” (4 points), “sometimes” (2 points) or “no” (0 points). The total score can vary from 0 to 100, and the scores, by domains, social and emotional, can vary from 0 to 48 and 0 to 52, respectively. The analysis and interpretation of the scores vary between total absence of the self-reported participation restrictions (0–16 points), presence of mild/moderate (18–42 points) and severe/significant (43–100 points).

Therefore, the researchers maintained the same score in the HHIE-adapted proposed by the original version, however they reformulated the questions in order to evidence hearing complaints related to socioemotional issues in situations without defined psychoacoustic alterations, so the assertions were not directed to a situation of hearing loss and its consequences, as in the original version.

The technique of choice for the application of the questionnaire was the “face to face” modality, which consists of the oral administration of the questionnaire by the researcher only with the reading of the items, after giving the instructions, without interferences of the interviewer. This was due to the fact that the sample presented heterogeneous characteristics of age group and schooling. The researchers conducted all questionnaire application with the CH patient in agreement with their respective caregivers, the latter assisting in the accuracy of the responses, confirming or complementing them, whenever necessary. As to the reliability of this technique, studies have shown satisfactory indexes for the results of self-reported participation restrictions (Weinstein et al., 1986; Carvalho and Iório, 2007).

Finally, the researchers extracted clinical and laboratory data from medical records. They adopted as criteria for the severity of CH the etiology of the disease (dysormonogenesis or dysgenesis). In addition to that, individuals were also classified as hyperthyrotropinemia positives when a discrete elevation of TSH levels (between 5.6 and 10 μ UI/mL) and normal free T₄ was detected (Brazil, 2012) at the serious dosage performed on the day of the audiological evaluation.

Thereafter, regarding adherence to treatment, they classified CHs as “hypertreated” and “hypotracted” when they had three or more episodes of serum TSH levels < 0.5 μ UI/mL or > 15 μ UI/MI (Lichtenberger-Geslin et al., 2013), respectively, with children who had at least 3 episodes of hormonal decontrol in the first 5 years of hormone replacement therapy, a period considered important for auditory maturation (Marti et al., 2006), in order to establish an association between hormonal control and the presence of self-reported participation restrictions.

2.4. Statistical analysis

The researchers conducted statistical analysis by using SPSS (Statistical Package for the Social Sciences) version 21 for Windows*. For descriptive statistics, continuous variables were described by median, strength of association and amplitude of upper and lower variance. They used The Student's t-test to determine the significance of the self-reported participation restrictions on inter- and intragroup. Finally, to verify the association between the self-reported participation restrictions and the clinical, laboratory and treatment-related variables, they used the Chi-square test for a significance level of 5% in order to reject the null hypothesis, with confidence intervals constructed with 95% statistical confidence. Fisher's exact test was adopted for the cases with expected values less than 5.

Table 1

Distribution of cases, in both study groups, of the percentage values, absolute and relative frequency of the values related to the self-reported participation restrictions scores, and their respective social and emotional domains, measured by HHIE-adapted.

Scores by groups	Distribution of HHIE-adapted scores						*p-value	
	n(%)	Mean (± SD)	Minimum Amplitude	Percentile (%)				Maximum Amplitude
				25	50	75		
Intergroups								
EG- Total score	26,0(62,9)	24,8(± 18,2)	0,0	12,0	20,0	37,5	64,0	** < 0,001
NEG- Total score	6,0(13,6)	10,0(± 7,2)	0,0	6,0	8,0	12,0	34,0	
Intragroup (EG)								
Emotional score	-	9,9(± 7,4)	0,0	4,0	8,0	16,0	28,0	**0,002
Social score	-	15,3(± 12,9)	0,0	4,0	12,0	23,0	44,0	
Intragroup (NEG)								
Emotional score	-	16,0(± 7,0)	0,0	9,5	16,0	20,5	28,0	0,104
Social score	-	11,0(± 3,5)	0,0	9,0	10,0	14,5	16,0	

Legend: HHIE-adapted –Hearing Handicap Inventory for the Elderly/Total –total score for self-reported participation restrictions (social + emotional)/EG, exposed group/NEG, non-exposed group/n- Absolute frequency of individuals who demonstrate some degree of auditory restriction/*The Student's t-test/**p < 0.05.

3. Results

The sample consisted of 86 individuals distributed in two distinct groups. 42 individuals with CH (50% female) formed the EG with median for chronological age and treatment time equal 8.5 years, and for age of neonatal screening age and treatment start in days for the CH of 21.5 (minimum 4 and maximum 92) and 55.6 (minimum of 16 maximum of 240), respectively.

44 individuals without a diagnosis of CH composed the NEG, median values for serum TSH levels 1.0 μ UI/ml and chronological age of 8.5 years. This group also presented an equivalence between the genders (50% female).

Regarding the findings of self-reported participation restrictions, in both groups, the EG individuals presented mean and percentage values in HHIE-adjusted scores higher than those of the NEG with a statistically significant difference (p < 0.001) (p = 0.002), as Table 1 demonstrate.

Fig. 1 shows the relative frequencies related to the total existence of self-reported participation restrictions in the exposed group, as well as their respective degrees of restriction presented, in descending order of frequency.

Analyzing the results of Table 2, the researchers observed a lack of statistical association between SRPR presence and the various degrees of self-reported participation restrictions with most of the clinical and laboratory variables related to adherence to treatment. However, there is a statistically significant association with irregular levels of TSH in the first five years of life (p = 0.039). In this last one, the “hypotracted” individuals showed higher prevalence rates of self-reported participation restrictions.

4. Discussion

The purpose of this study was to verify evidence of auditory alterations in the subclinical condition in individuals affected by CH, normo-hearing, by measuring the existence of the self-reported participation restrictions in this population, based on the comparison of individuals without the disease. Through this study design, it was possible to observe the significant existence of the SRPR individuals with CH, with greater relevance to the social aspects when compared to the emotional ones.

These findings attest to the influence of the most common metabolic disorders of childhood on the auditory mechanisms. They suggest that there are still factors intrinsic to the disease that are unknown, but that

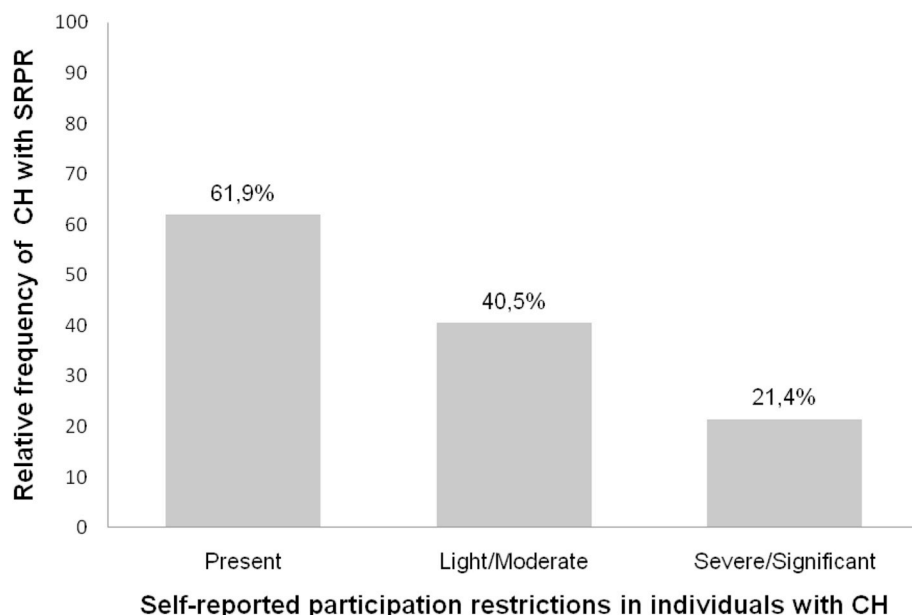


Fig. 1. Distribution of the total presence and classification of the degree of self-reported participation restrictions in the exposed group, in relative frequency, measured by HHIE-adapted (n = 42).

Legend: HHIE-adapted –Hearing Handicap Inventory for the Elderly/SRPR - self-reported participation restrictions/CH –Congenital hypothyroidism.

present enough potential to interfere in the adequate functioning of the auditory pathways, although at a preclinical level, as well as during the early treatment of hormone replacement, justifying the high frequency of hearing impairment in the present study.

The researchers observed similar findings in a group of normal hearing individuals with type 1 diabetes mellitus (DM1) (Fernandes et al., 2014). Although the pathogenesis between DM1 and CH is completely different, these data corroborate with the discussion about the deleterious effects on the auditory system in the presence of a

childhood metabolic disease, which indicated the need for further investigation in this area.

In addition, presence of SRPR has also been reported in cases of thyroid hormone resistance (THR⁺) (Brucker-Davis et al., 1996), where 5% of the sample had some degree related to this restriction. This evidence corroborates with the theory of the important function of the THs in the auditory system, and it strengthens the hypothesis of the influence of the time of impairment, since the prevalence of the self-reported participation restrictions in THR⁺, a condition of common

Table 2

Distribution of prevalence rates (%), median and range of presence of self-reported participation restrictions in the exposed group and associations with clinical and laboratory variables related to the treatment of congenital hypothyroidism.

Clinical and laboratory aspects	Self-reported participation restrictions				
	Median	Amplitude (min-max)	↑ (%)	PR [95% CI]	p-value [‡]
Gender					
Male	20	00-64	61,9	1	0.375
Female	18	02-52	61,9	1.0 [0.62-1.61]	
Time of illness/treatment					
≤ 8 (yearsold)	20	00-64	61,9	1	0.375
> 8 (yearsold)	20	00-60	61,9	1.0 [0.62-1.61]	
Age – CH Neonatal Screening					
≤ 7 (days)**	20	00-54	71,4	1	0.489
> 7 (days)	20	00-64	63,0	0.88 [0.51-1.53]	
Age - Beginning of CH treatment					
≤ 28 (days)**	26	00-54	85,7	1	0.177
> 28 (days)	19	00-64	57,7	0.67 [0.43-1.05]	
Etiology of CH					
Non-dysgenesis	20	00-64	64,5	1	0.411
Dysgenesis	19	00-52	54,5	0.85 [0.46-1.54]	
Hyperthyrotropinemia					
Absent	20	00-64	60,0	1	0.492
Present	17	00-54	50,0	0.83 [0.37-1.87]	
Treatment condition					
Normo-treated (0,5 - 15 µUI/ml)	26	00-64	78,6	1	
Hypertreated (< 0,5 µUI/ml)	16	00-44	41,2	0.52 [0.28-0.98]	0.042*
Hypotreated (> 15 µUI/ml)	20	16-54	85,7	1.09 [0.85-1.45]	0.422

Legend: SRPR- Self-reported participation restrictions; Min- Minimum amplitude of the score; Max- Maximum amplitude of the score; † - Prevalence rate corresponding to the presence of SRPR; ‡ Chi-square test of association; *p ≤ 0.05.

Note: ** Age limit recommended by the Ministry of Health, by the Unified Health System, as appropriate for the beginning of the treatment of congenital hypothyroidism.

occurrence in adulthood, was lower than found in individuals affected by CH, which constitutes an endocrinopathy of origin, still, in the intrauterine life.

Therefore, the social domain seems to suffer a significant gap in CH, which can lead to a deterioration of the quality of life, since individuals with difficulty to listen tend to involuntary social isolation for fear of facing routine situations in their community (Wieselberg and Sousa, 2013), as well as fear of imminent rejection in a communicative environment.

The fact that there is less frequency of hearing-related emotional imbalance in this study, as well as in other studies with the same theme (Menegotto et al., 2011; Baruzzi et al., 2009; Weinstein et al., 1986; Carvalho and Iório, 2007), may be related to a secondary function of this domain for some daily auditory situations or for being masked by psychophysiological changes, when compared to the social aspects, although both domains are mutually dependent, especially when it comes to individuals at an early age, a period of full exploitation of the surrounding environment.

Therefore, stress and anxiety due to hearing problems are more relevant in cases of noise-induced loss or in association with cochlear-vestibular symptoms such as the perception of the tinnitus (Pajor et al., 2013; Canlon et al., 2013), although there is also a significant association between hearing loss and depression (Bernabei et al., 2011), which impairs the performance of their daily living activities.

Additionally, it is worrisome to the existence of varying degrees of self-reported participation restrictions in a sample composed exclusively of normo-listeners, where almost half of the individuals had a mild/moderate degree, divided into the social and emotional scales, not expected when dealing of a population where there is no lowering of the auditory threshold and abnormalities of the cochlear function (Aiello et al., 2011).

In agreement with the findings, researchers who evaluated hearing of a sample of individuals submitted to total thyroidectomy at the pre and postoperative moments, in order to analyze the acute effect of the deflection of the HTs at the hearing, demonstrated that hypothyroidism can cause elevation of pure tones in humans and, to a greater degree, the recording of the OAE signal, indicating subclinical involvement of the cochlear function (Psaltakos et al., 2013).

These findings confirm the suspicion of signs of subclinical alterations (Rocco et al., 2015) that may be related not only to structural alterations in peripheral sites but also involving the auditory sub-processes of the auditory pathways, such as auditory skills related to the central auditory processing, which would justify the significant effect on the self-reported participation restrictions in the emotional and, especially, social domains (Baruzzi et al., 2009; Fire et al., 1991).

Although there is no expected degree of self-reported participation restrictions in individuals with normal hearing, the presence of the mild/moderate degree is a more acceptable situation, due to the specifications already mentioned above, to the detriment of the more advanced degrees, practically exclusive to groups with hearing impairment, especially those with greater deterioration in speech frequencies. However, there was a record of the presence of the severe/significant degree in this study, since it could be interpreted as an incompatible finding or result of an information bias.

Furthermore, it is well known in the literature that SRPR and auditory thresholds are often discordant because psychoacoustic measurement by pure tone is not sufficient to quantify the variables dependent on social, emotional and communicative experiences in the various everyday situations and, even, the adaptive capacity to a hearing alteration (Hallberg et al., 2008; Helvik et al., 2006).

Thus, individuals with similar auditory thresholds may demonstrate different SRPRs (Aiello et al., 2011). However, other disorders that are located at the most central sites of the auditory pathways that the basic hearing tests cannot detect must not be discarded. These evidences demonstrate the need not only to evaluate the peripheral processes of

hearing but also the auditory subprocesses through standard verbal and non-verbal stimuli as well as electrophysiological examinations of medium and long latency.

The researchers expected the results presented in this study, since the presence of the prevalence of otoneurological symptoms (Andrade et al., 2017), as well as previous complaints related to acoustic signal processing disorders (Andrade et al., 2018) in CH, have already been documented in the literature. Moreover, the higher frequency of the self-reported participation restrictions for the social domain explains the constant learning difficulties and communicative abilities (Gejão et al., 2009) and, therefore, the common reports of academic failure experienced by CH patients.

The researchers also observed that the clinical aspects related to the hormonal decontrol during the first five years of treatment of patients with CH had a statistically significant association with the high presence rates of self-reported participation restrictions ($p = 0.042$), suggesting that inadequate levels of TSH due to poor administration in hormone replacement may be contributing to the prevalence of restriction of participation in activities of daily living in CH.

Proper hormone replacement is essential in order to prevent the beginning of deleterious effects in individuals with CH. In cases of overdose of levothyroxine sodium, symptoms of thyrotoxicosis appear, as well as the possibility of advancing bone age when maintained for a prolonged period. On the other hand, impairment to growth and neuropsychomotor development may occur during the period of under dosing, especially when maintained over a long period of time (Brazil, 2012). In this last one, it points out the high prevalence rates of hypotreated individuals (85.7%) with self-reported hearing impairment.

The importance of the aforementioned findings serves to draw the attention of the professionals involved in the treatment of CH to the need to include detailed audiological evaluation in the clinical routine of these patients, in addition to the implementation of a system for monitoring hearing health, language development and success since the largest portion of the sample of subjects with CH without peripheral auditory alterations in this study presented some degree of self-reported participation restrictions.

These data also indicate that despite the improvements in the diagnosis, treatment and prognosis of CH patients after the advent of Neonatal Screening Programs, hearing alterations, although more subtle, remain a hearing health problem (Rocco et al., 2015) in the subclinical modality and that, if not identified and treated in time, can evolve to the clinical form, generating several deleterious effects to the individuals.

Finally, due to the lack of studies with a study design similar to the present study, there were some limitations related to the bibliographic collection in order to discuss and compare the results found, which are inherent in all the research processes that assume the risks of adopt an unprecedented methodology to explore and to know more in detail its object of study.

This research intends to contribute to broaden the knowledge regarding the deleterious effects of the CH in the auditory system, as well as to assist all the professionals involved in the treatment of CH and to add, in the scope of its clinical practice, new technologies as support to expand the evaluation of the auditory health of these patients. In addition, to instigate other studies in the area with the goal to aggregate new knowledge about the subject.

5. Conclusion

The findings suggest that normal hearing individuals affected by CH have a significant self-reported participation restriction, of varying degrees, suggesting evidence of auditory abnormalities in the sub-clinical condition, which presented an important relation with the hormonal decontrol during the treatment in individuals.

Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.joto.2018.11.007>.

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