

Cancer treatment: changes in hearing thresholds

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Abstract

Purpose: Evaluate changes in hearing thresholds in patients undergoing cancer treatment.

Method: Prospective, longitudinal study carried out at Cancer Center of a Sergipe's public hospital, Brazil. Audiological evaluation (Conventional Pure Tone Audiometry) have been performed in 20 patients following eight weeks of cancer treatment (reference exam) and 20 weeks (sequential exam) of treatment. All survivors had normal hearing thresholds before cancer treatment. The procedure has been approved by the Ethics in Research Committee, under protocol # 33665014.7.0000.5546.

Results: Head and neck cancer displayed oncology highest incidence (35%). Referential exam, eight weeks before treatment, displayed 15% with sensorineural hearing loss and 17.5% at second tests. It was observed a slight worsening for all test frequencies of referential and sequential exam. Tinnitus was the biggest complaint (81.3%), but there was no statistic correlation between hearing loss ($p=0.89$).

Conclusion: Hearing monitoring from this small sample suggest chemotherapy and radiotherapy treatments can have a detrimental effect on hearing thresholds significate for 2 to 8kHz eight weeks after cancer treatment and 4 to 8kHz 20 weeks before.

Introduction

Since 1960, cancer has been the major cause of death in the world. The estimation of this disease in Brazil for 2019 is 600 thousand of new cases. In Aracaju (Brazilian north east), numbers have been increasing significantly, once INCA notified 3.610 cases in 2010 and in 2014, 4.755 cases [1]. For 2018/2019 there will be an estimation of 4.930 new cases in Aracaju, Sergipe.

Treatment methods have been widely used. There is an increase of successful outcomes and the cure of some cancers is well documented. Despite it, chemotherapy and radiotherapy lead to deleterious collateral effects. One of them is hearing loss, which can affect middle or inner ear [2]. Generally, hearing loss is sensorineural, bilateral and irreversible, tends to be permanent and it has tinnitus as a symptom [3,4]. It is a result of ototoxicity, which can damage cochlea's basal turn and hits outer hair cells, before some days or weeks after cancer treatment [5].

It is essential to follow-up patient's hearing system. Hearing loss affects either communication, social and emotional aspects; it may further reduce quality of life. Moreover, investigators have described hearing loss during cancer treatment, which can become worse (75% up to a 100%) especially in higher frequencies [3,5]. Audiological procedure, as conventional pure tone audiometry, is the basic of audiological battery for hearing loss diagnostic, once ototoxicity can develop a high frequency damage [6].

Early diagnosis and hearing assessment is essential to identify the hearing loss early. It reduces impact on the individual's life by means of proper medical and hearing intervention [7]. However, it is difficult to monitor hearing thresholds, once most of patients are

debilitated and die before finishing treatment, that's why there are few studies with longitudinal audiological follow-up [8].

The aim is to evaluate changes in hearing thresholds of patients undergoing cancer treatment.

Method

Prospective, longitudinal, transversal cohort study has been carried out at a Public Hospital in Aracaju, Brazil. The Ethics and Research Committee approved it under protocol #33665014.7.0000.5546. All patients agreed to undergo hearing test, and all provided written informed consent for participation in this study.

It was recorded serial audiometric evaluations of 20 cancer treatment's patients in two years (2015/2016). All patients came from free demand or by medical referral. To be part of the research, all participants should have medical cancer diagnosis, be on chemotherapy and/or radiotherapy treatment and have a normal hearing threshold before the cancer treatment.

Patients who had ear surgery, history of acoustic noise-induced hearing loss trauma, ear infections, congenital syndromes and obstruction of the external acoustic meatus and those who previously had received

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chemotherapy and/or radiotherapy treatment were excluded from the study.

As a procedure, anamnesis and conventional pure tone audiometry were part of the evaluation.

Researchers have developed an anamnesis to collect patient's medical history as previous history of cancer (age at diagnosis, type and extent of disease, type of treatment, symptom) and hearing aspects (hearing complaints and previous otological history).

Hearing threshold (air conduction) were recorded across all octave frequencies from 250 to 8.000Hz. Bone conduction test was recorded for all patients between 0.5 to 4kHz frequencies. A hearing threshold of 26 dB HL was considered significant for hearing impairment, so hearing threshold 0-25dB HL was defined as normal. Mild, moderate, severe and profound hearing loss were defined as hearing thresholds in the range of 26-40dB HL, 41-70dB HL, 71-90dB HL and +91dB HL, respectively [9]. Audiology records were taken with a pure tone-screening audiometer Ad28 (Interacoustics, Denmark) with TDH 39 earphones.

Two audiograms were acquired during the treatment: referential (first exam) was collected eight weeks before the cancer treatment and sequential exam (second exam), 20 weeks before. During the treatment, all patients were receiving chemotherapy and radiotherapy. Referential exams were compared with sequential exam based in American Speech-Language-Hearing Association criteria (ASHA, 1994). Comparing the two exams, it was considered normal or acceptable variability in hearing threshold a difference of 10 dB HL in a single frequency; variability more than 20 dB HL in a single frequency or 10 dB HL in two or more frequencies was considered thresholds increase [10].

The data analysis for this study was generated using Statistical Package for Social Sciences 20 version (SPSS, Chicago, USA). Normality of distribution was assessed using the Kolmogorov Test. Relationships of continuous variables with the presence/absence of hearing loss were valuated with the Mann Whitney Test, while categorical data were compared using the Chi-squared test. P values of less than 0.05 were considered statistically significant.

Results

The present study of audiological assessment set out 20 cancer patients, whose average age were 33.5 (± 15.66) years, 55.5% were female, 35% had head and neck cancer and 15% breast cancer.

Tinnitus was present in 81.3% of all patients with no significant difference between those who had hearing loss and normal hearing thresholds ($p = 0.11$; Chi-square Test). During the treatment, at sequential exam, 20% reported that tinnitus gets worse.

Audiological findings displayed 15% with sensorineural hearing loss as from 3kHz frequency at referential exam. 28.8% of head and neck cancer's patients were diagnosed with hearing loss. Data analysis revealed a statistical significant difference between those who had hearing loss and normal hearing thresholds from 2 up to 8kHz in referential exam (Figure 1).

Figure 2 describes sequential audiological findings. It was diagnosed 17.5% with sensorineural hearing loss with statistical significant difference between hearing loss and normal hearing thresholds from 4 up to 8kHz.

The comparison of referential and sequential exams by ASHA (1994) criteria demonstrated that 35% of audiograms had increased hearing thresholds. One patient had a normal hearing threshold in referential exam, but the sequential exam displayed hearing loss.

Moreover, normal hearing thresholds had a statistical significant difference of 4kHz between referential and sequential exam (Figure 3).

On the other hand, patients who was diagnosed with hearing loss in referential exam had equal audiological findings in sequential exam, except for 0.25 kHz. There was a statistical significant difference of 0.25 kHz between referential and sequential exam (Figure 4).

Discussion

The incidence of cancer type was 35% for head and neck in male. Head and neck cancer occupies the fifth position of all men's cancer. There is association of this type of cancer with tobacco and alcohol

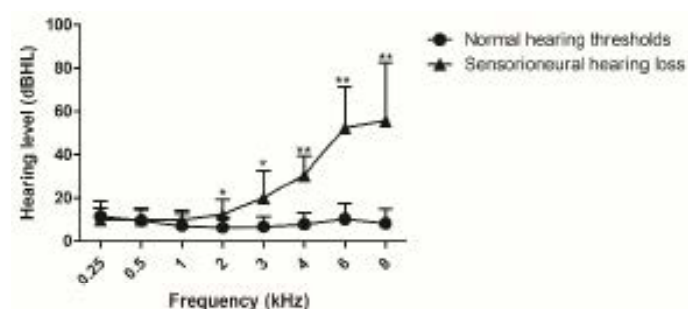


Figure 1. Referential hearing thresholds, as measured by conventional pure tone audiometry evaluated five weeks after cancer treatment. Normal hearing threshold $n=34$ and sensorineural hearing threshold $n=06$. For analysis, Mann Whitney test was used. Values are expressed as mean \pm SD. (*) $p < 0.05$ and (**) $p < 0.01$ vs. normal hearing threshold. dB HL: decibel hearing level

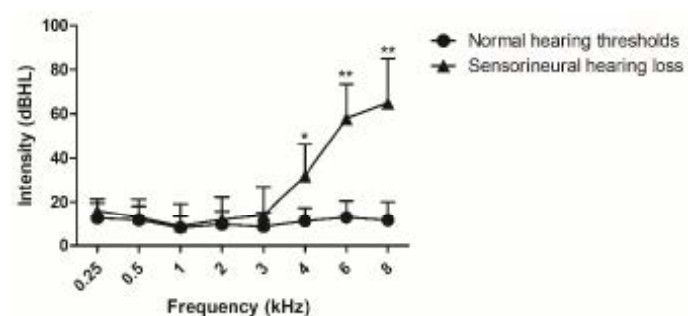


Figure 2. Sequential hearing thresholds, as measured by conventional pure tone audiometry evaluated ten weeks after cancer treatment. Normal hearing threshold $n=33$ and sensorineural hearing threshold $n=07$. For analysis, Mann Whitney test was used. Values are expressed as mean \pm SD. (*) $p < 0.05$ and (**) $p < 0.01$ vs. normal hearing threshold. dB HL: decibel hearing level

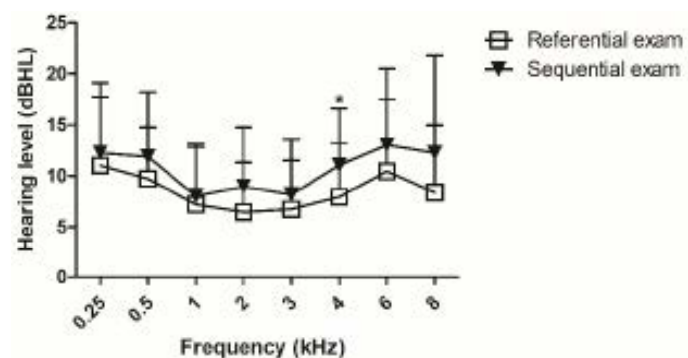


Figure 3. Normal hearing thresholds of referential and sequential exams, as measured by conventional pure tone audiometry. Referential exam $n=34$ and sequential exam $n=33$. For analysis, Mann Whitney test was used. Values are expressed as mean \pm SD. (*) $p < 0.05$ vs. referential exam. dB HL: decibel hearing level

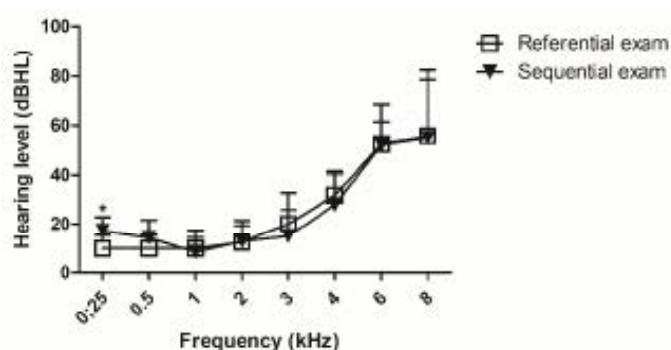


Figure 4. Hearing loss thresholds of referential and sequential exams, as measured by conventional pure tone audiometry. Referential exam n=06 and sequential exam n=07. For analysis, Mann Whitney test was used. Values are expressed as mean \pm SD. (*) $p < 0.05$ vs. referential exam. dB HL: decibel hearing level.

consumption [11]. On the other side, in our study, women were diagnosed with breast cancer (15%). Studies reported high incidence of breast cancer in women and it is the fourth most common oncologic diagnose in adults [11,12].

Hearing loss was diagnosed in 15% of all cancer patients. There is a variability of hearing loss incidence, once it has influence of radiation technique (2D or 3D) and dose, anticancer drugs and dose, individual susceptibility and age [3,13]. In our research, all patients received, and 3D radiotherapy as prescribed by oncologist. As chemotherapeutic drugs were carboplatin, cyclophosphamide and doxorubicin, which can damage permanently organ of hearing as described [3,14,15]. Investigators described that platinun drugs affected 14% of cancer treatment's survivors once these drugs are considered not only ototoxic, but neurotoxic [15]. The incidence of hearing loss for head and neck cancer, in our study was 28.8% therefore investigators reported an incidence of 27% to 95% [13].

Our audiometric configuration results were characterized by sensorineural hearing loss. Indeed, investigators reported that most of hearing loss in oncology survivors is sensorineural [5,16-18], which affects inner ear, particularly outer hair cells [3,17]. Inner ear is the most susceptible organ in a durable long-term radiotherapy and chemotherapy. Cancer treatment leads to an inner ear vascular insufficiency, reduces number of capillaries, degenerates endothelial vessels, loss of cells of Organ of Corti, degenerates striavascularis and leads to spiral ganglion cells and cochlear nerve atrophy [6,19].

Radiotherapy is the most common treatment for head and neck cancer, initially patients can have acute middle ear side effects; therefore, they can develop an inner ear hearing loss. As described, chemotherapy uses drugs like Cisplatin, Carboplatin, Oxaliplatin, and Nedaplatin, which have been widely chosen as an efficient treatment in oncology. Moreover, platinun group is the most devastating drug to inner ear [3,14,15]. It has toxic side effects to the peripheral auditory system which lead to hearing loss with an impaired social communication [3].

A large number of patients, in our research complained about tinnitus (81.3%). Tinnitus is a common condition, especially in cancer treatment, caused by chemotherapy drugs and radiotherapy [17,20-22]. The present study did not reveal relation between tinnitus and hearing loss, in contrast investigators have reported this relation [20]. Chemotherapy with platinun and / or taxane compounds develops neurotoxicity, which induces neuropathy. Investigators reported hearing loss, balance problems and tinnitus with significant decrement of quality of life [15].

The incidence of hearing loss was observed at frequencies above 3KHz, in our study. Indeed, investigators reported hearing loss at high frequencies [5,8,23]. Only radiotherapy as head and neck cancer treatment reported hearing loss at frequencies above 4kHz [13].

In our study, follow-up exams showed that 15% had sensorineural hearing loss in referential exam and it increased to 17.5% (sequential exam). One study reported a 75% of hearing thresholds worsening [7]. Most of studies evidenced that hearing thresholds during cancer treatment get worse [5,7].

Conclusion

The results from this small sample suggest that chemotherapy and radiotherapy treatments can have a detrimental effect on hearing thresholds from 4 to 8kHz eight weeks before cancer treatment and 2 to 8kHz 20 weeks after.

Authorship and contributions

Machado, L.A.R, Amaral, T.S, Aguiar, L.K.S participated in audiometric evaluation procedure. Oliveira, A.C participated in the statistical analyses and discussion of results. Oliveira, P.F. conducted the research and participated in all stages of manuscript preparation.

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Declaration of interest

The authors report no conflicts of interest.

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