



Assessment of auditory functions in chronic hepatitis C patients treated by sofosbuvir

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ABSTRACT

Objective: Evaluating the auditory function in patients with chronic hepatitis C treated with sofosbuvir and ribavirin.

Methods: This study involved 80 patients with chronic hepatitis C who agreed to receive sofosbuvir and ribavirin. All participants were subjected to baseline otological and audiological assessment just before treatment. The audiological assessment included standard pure tone audiometry, extended high-frequency audiometry, immittance and otoacoustic emissions (OAEs) (transient and distortion product). According to baseline hearing threshold measurements, the study population was divided into 2 groups. Group 1 included 42 patients with normal hearing sensitivity (250–8000 Hz), and Group 2 included 38 patients with sensorineural hearing loss. After 24 weeks of therapy, otological and audiological assessments were repeated and compared between the two groups and before and after therapy.

Results: Post-treatment hearing threshold evaluation showed no significant difference from pretreatment evaluation at all tested frequencies. There was no statistically significant difference between pre and post-treatment otoacoustic emissions results.

Conclusion: Therapy with sofosbuvir and ribavirin in chronic hepatitis C has no noticeable effects on cochlear functions.

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1. Introduction

Chronic hepatitis C is considered as a global public health problem that affects about 300 million people worldwide (Raja and Janjua, 2008) with three to four million people infected per year (Berenguer et al., 2001). Chronic hepatitis C causes inflammation of the liver with consequent liver function impairment or liver failure. In 2015, an Egyptian national health issue survey was performed to determine the prevalence of hepatitis C virus (HCV) infection. In the 15–59 years age group, the prevalence of HCV antibody was 10.0% and that of HCV RNA was 7.0%. In children (1–14 years), the prevalences of HCV antibody and HCV RNA were .4% and 0.2% respectively. In 2015, approximately 3.7 million people between 15 and 59

years of age had chronic hepatitis C (Kandeel et al., 2017).

For many decades, the standard of care treatment of chronic HCV infection was PEG-interferon and ribavirin combination therapy. Until 2011, the approved therapy for chronic HCV infection was the combination of pegylated interferon (Peg IFN) - and ribavirin for 24 or 48 weeks according to virus genotypes (European Association for the Study of the Liver, 2012). It is well known that this combination is associated with significant adverse effects. Unilateral or bilateral sensorineural hearing loss (SNHL) has been reported as a consequence of treatment with both non-pegylated and pegylated interferons. Sudden hearing loss may occur in about 1% of patients on PEG-IFN/ribavirin combination therapy (Piekarska et al., 2007).

The reported incidence of hearing loss associated with interferon treatment ranges from 0.1% to 39.5% (Kanda et al., 1995; Okanoue et al., 1996). Shehata et al. (2013) studied the effect of interferon and ribavirin on hearing in 50 patients with chronic HCV infection and reported no noticeable change in audiometry readings in 30 cases (60%) and SNHL in 20 cases (40%), of whom 10 recovered completely, 8 (16%) showed partial recovery and 2 (4%)

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were auditorily disabled. Also, [Asal et al. \(2015\)](#) reported significant elevation in hearing thresholds at the 12th and 24th weeks as compared to at the onset of the study in patients treated with interferon and ribavirin, with mostly higher frequencies being affected (3000, 4000, 6000, 8000, 9000, 10 000, 11 200, and 12 500 Hz), although otologic complaints in these patients were insignificant, except for tinnitus. A significant increase in tinnitus was observed from 0 to 31.1% by the end of the study.

The U.S. Food and Drug Administration has recently approved oral-directly acting-drugs against chronic HCV virus infection. Sofosbuvir (Sovaldi®) is a nucleotide analog NS5B polymerase inhibitor indicated for the treatment of genotypes 1, 2, 3 and 4 chronic HCV virus infections as a component of a combination of antiviral treatment regimens. Fatigue and headache were the most common side effects reported by participants in the clinical study who were treated with sofosbuvir and ribavirin ([Food and Drug Administration, 2015](#)). Although sofosbuvir is FDA approved, no studies have been conducted to assess the cochlear function in HCV infected patients treated with this drug, despite the fact that multiple studies reported auditory impairments in previous HCV treatment regimens.

Moreover, chronic HCV infection is endemic in Egypt and there is a national campaign to eradicate this virus. The Egyptian Ministry of Health guidelines for HCV therapy do not include hearing screening programs by audiometry or monitoring cochlear function during treatment or in follow-up protocols.

To the best of our knowledge, no studies have been conducted to evaluate the effect of sofosbuvir on auditory functions in chronic hepatitis C patients. Accordingly, this work was designed to evaluate the effect of sofosbuvir in combination with ribavirin on cochlear functions in patients with chronic hepatitis C, via standard audiological evaluation, extended high-frequency audiometry and otoacoustic emissions.

2. Material and methods

This prospective cohort study identified 119 chronic HCV infected patients assigned to receive sofosbuvir and ribavirin therapy. They were recruited from January 2015 to September 2016 in the Tropical Medicine Department outpatient clinic and referred to the audiology unit. This study was performed after fulfilling the requirements of Mansoura ORL Department Ethical Committee and was approved by the Institutional Research Board of Faculty of Medicine, Mansoura University. All patients presented written informed consent in accordance with the Declaration of Helsinki. All patients were diagnosed to be HCV positive on the basis of persistence of positive HCV-RNA for more than 6 months. All patients underwent baseline assessment including thorough history intake, physical examination, complete blood count (CBC), liver enzymes, serum creatinine, international normalized ratio (INR), α -fetoprotein, polymerase chain reaction (PCR) for HCV RNA, abdominal ultrasound, and electrocardiogram. Inclusion and selection of drug regimen were based on EASL and AASLD International guidelines and Egyptian national guidelines for treatment of chronic HCV infection 2015/2016. Exclusion criteria included treatment of chronic hepatitis C with sofosbuvir-based regimens, severe renal impairment (creatinine clearance ≤ 30 ml/min), pregnancy, unwillingness to comply with adequate contraception, and decompensated liver diseases. Patients who had one or more of the following conditions were also excluded from this study: medical or neurological problems known to affect the auditory system, family history of hearing impairment, ototoxic drug intake and noise exposure. Patients were required to have no history of chronic middle ear pathology, otological complaints, ear operation, or otoscopic evidence of ear-drum abnormalities.

3. Equipment

1. Two channel audiometer (Interacoustic AC40 diagnostic audiometer, version 1.48, Denmark) with HAD 200 high-frequency headphones. The audiometer and HD 200 headphone were calibrated using IEC60318 with type 1 adaptor coupler. The maximum output of the EHF audiometer was 100, 90, 80, 60, 30, 15 dB HL at 10, 12.5, 14, 16, 18, 20 KHz respectively;
2. Locally manufactured sound-treated chamber;
3. Immittanceometry (GSI, tymstar, middle ear analyzer version 2 with 226 Hz probe tone, USA) and
4. Otoacoustic emissions (Biologic Scout OAE, Natus hearing diagnostic version 4.0 USA)

4. Procedures

Each patient was subjected to a full assessment of history including any otologic complaints in the form of hearing loss, tinnitus, vertigo or otalgia, which were assessed before starting therapy and at the end of the follow-up period (24 weeks). Of the 119 candidates, only 93 met our selection criteria; while 14 had abnormal middle ear function and 12 had absent transient otoacoustic emissions (TEOAE) (3 bilateral and 9 unilateral) and had to be excluded from the study. Patients then were followed monthly during the course of treatment (24 weeks) for any side effects caused by the drug regimens with special attention paid to auditory symptoms.

All patients also underwent an otoscopic examination. An audiological evaluation was carried out within a week before starting therapy and at the end of follow-up. It included the following: (1) Pure tone (PT) audiometry in the form of standard audiometry, which included air conduction thresholds at conventional test frequencies (0.25, 0.5, 1, 2, 4 and 8 kHz); (2) Speech audiometry, including speech reception threshold, using Arabic spondaic words ([Soliman, 1976](#)), and the word discrimination score (WDS), using Arabic phonetically balanced monosyllabic word lists ([Soliman et al., 1985](#)). Twenty-five words were used to test each ear and scores were expressed in percentage; (3) Extended high frequency (EHF) audiometry at 10, 12.5, 14, 16, 18 and 20 kHz using the same audiometer; (4) Tympanometry was performed and ipsilateral and contralateral acoustic reflex thresholds were obtained; (5) Otoacoustic emissions (OAEs) including (a) transient-evoked otoacoustic emissions (TEOAEs) induced by clicks (80 dB pe SPL) at 1, 1.5, 2, 3 and 4 kHz in a 20-ms window; and (b) distortion product otoacoustic emissions (DPOAEs) in the form of a DP-Gram over $f_2 = 750, 984, 1500, 2016, 3000, 3984, 6000$ and 7969 Hz ($L_1 = 65$ dB SPL and $L_2 = 55$ dB SPL, $f_2/f_1 = 1.22$). TEOAEs were considered present if response signal to noise ratio (SNR = otoacoustic amplitude minus noise floor in dB SPL) was ≥ 6 dB with reproducibility $> 70\%$ at least in three frequencies with overall $SNR \geq 6$ dB SPL and overall reproducibility $> 70\%$.

Patients were divided into 2 groups basis on standard pure tone audiometry (PTA) results at the beginning of the study: Group (1) i.e. patients with normal hearing sensitivity over 250–8000 Hz (Group 1), of whom 42 completed follow-up; and patients with SNHL in the frequency range of 250–8000 Hz (Group 2), of whom 38 completed follow-up. The 80 patients who completed the follow up were included in data analysis. We had no sex restrictions in our study.

5. Statistical analysis

Data were analyzed using the Package for Social Science software version 17 (SPSS, Inc., Chicago, IL, USA). Quantitative

parametric data were presented in mean and standard deviation, while nonparametric data were presented in median and interquartile range (IQR). For quantitative parametric data, Student's t-test (Unpaired) was used to compare between two different groups and paired Student's t-test was used to compare between two related groups. For non-parametric data, Wilcoxon signed rank test was used to compare between two related groups. Chi-square was used to compare qualitative data. A p-value less than 0.05 was considered statistically significant.

6. Results

Chronic HCV assigned to receive combined therapy (sofosbuvir + ribavirin) completed the study, including 42 with normal hearing, of whom 18 (42.9%) were men and 24 (57.1%) were women, and 38 patients with SNHL, of whom 14 (36.8%) were men and 24 (63.2%) were women. There was no statistically significant difference between the two groups regarding sex. The mean age was 39.81 years ± 8.91 for Group 1 (normal hearing group) and 58.68 years ± 3.32 for Group 2 (SNHL group) (P < .001) (Table 1).

Test used: Student's t-test (unpaired) for data expressed in mean ± SD and Chi-square for data expressed in number or percent.

There was no statistically significant difference between the right and left ear as regard to standard pure tone audiometry, extended high-frequency audiometry, TEOAE and DPOAE results (p > .05).

There was no statistically significant difference in standard audiometric (Table 2) or extended high-frequency audiometric results (Table 3) for all tested frequencies before and after treatment.

Differences in speech reception threshold (dB) and WDS (%) were statistically insignificant and all patients had excellent WDS both before and after 24 weeks of treatment in both groups. No patient in this study developed tinnitus, hearing loss, vertigo or otalgia. There was no complaint of difficulty in speech discrimination in a noisy situation in any patient participating in this study pre or post-treatment. In addition, all patients included in the study had normal middle ear functions with ipsi- and contralateral acoustic reflexes proportionate to PTA threshold both pre- and post-treatment.

When before and after treatment results were compared, standard pure tone audiometry (Table 4) and extended high-frequency audiometry (Table 5) in both groups showed no statistically significant difference.

TEOAE and DPOAE are listed in Tables 6 and 7, and also showed no statistically significant difference in both groups before and after 24 weeks of treatment (Tables 8 and 9).

7. Discussion

Hepatitis C virus (HCV) infection remains an important etiology of chronic liver diseases worldwide. Treatment of HCV infection

Table 1
Age and gender comparison between the two study groups.

Item	Chronic hepatitis C with normal hearing (n = 42)		Chronic hepatitis C with SNHL (n = 38)		P	
	Mean	±SD	Mean	±SD		
Age	39.81	8.91	58.68	3.32	<.001*	
	No	%	No	%		
Sex	F	24	57.1%	24	63.2%	>.05
	M	18	42.9%	14	36.8%	

SD = standard deviation P = Probability *P < .05.

Table 2
Pre- and post-treatment standard audiometric thresholds (dB HL) in patients with normal hearing and patients with SNHL.

Frequency Hz	Hepatitis C with normal hearing				Hepatitis C with SNHL			
	Before treatment		After Treatment		Before treatment		After Treatment	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
250	12.33	2.97	12.86	2.99	23.42	8.83	23.68	8.79
500	12.14	3.73	11.90	2.95	27.11	9.18	28.42	9.44
1000	10.95	3.01	9.29	3.64	30.00	12.58	31.05	9.22
2000	10.48	3.50	11.43	3.22	37.37	7.88	38.68	7.97
4000	11.19	4.15	11.90	3.35	44.21	8.21	46.84	6.91
8000	12.76	4.38	12.14	5.14	50.26	11.96	52.11	10.71

Table 3
Pre- and post-treatment extended high frequency audiometric thresholds (dB nHL) in patients with normal hearing and patients with SNHL.

Frequency kHz	Hepatitis C with normal hearing				Hepatitis C with SNHL			
	Before treatment		After Treatment		Before treatment		After Treatment	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
10 kHz	11.1	3.83	10.9	4.79	44.3	4.83	44.9	4.9
12.5 kHz	12.1	3.8	11.1	3.44	47.5	4.8	47.1	3.44
14 kHz	12.2	4.78	12.3	3.92	49.3	4.8	48.3	4.32
16 kHz	12.1	3.06	11.9	3.97	51.2	3.4	52.03	2.97
18 kHz	10.8	3.71	11.2	3.91				
20 kHz	10.4	3.2	10.1	3.99				

The hearing thresholds in Group 2 (with SNHL) exceeded the output limit of the audiometer at 18 and 20 kHz.

using pegylated-interferon and ribavirin was less than effective and accompanied by numerous side effects. Direct-acting antivirals (DAAs) used today are considered a better treatment. The first-generation DAAs improved efficacy but also were associated with substantial side effects. The next generation of DAAs (simeprevir and sofosbuvir) have improved the efficacy of the regimens with a considerably safer profile. Sofosbuvir is an HCV-specific uridine nucleotide analog that inhibits the NS5B polymerase (Lam et al., 2014).

In the current study, the age difference between the two study groups seems to indicate that hearing loss in the group of SNHL likely represents presbycusis which is a disease of aging.

In our study, during history taking, we ensured that all patients reported a detailed history of tinnitus, vertigo or otalgia. By the end of the 24 weeks of therapy, none of our patients developed tinnitus, hearing loss, vertigo or otalgia. Tinnitus has been reported to be a common side effect of many ototoxic drugs, and there is a common assumption of tinnitus as an early indicator of ototoxicity (Seligman et al., 1996).

Hearing loss due to ototoxic drugs usually affect the highest frequencies first, and as drug use continues lower frequencies become affected. As standard audiometry measures up to 8 kHz, it may not identify initial cases of hearing loss from ototoxic drugs (Bisht and Bist, 2011).

In the present study, post-treatment hearing thresholds at frequencies from 0.25 to 20 kHz showed no significant difference from pretreatment evaluation, indicating no hearing impairment at these frequencies.

The sensitivity of OAEs as an early indicator of cochlear dysfunction in patients receiving ototoxic agents has been recorded. Reduction in OAE amplitude, as an early sign of an ototoxic effect, may be attributed to outer hair cell (OHC) damage (Youssef,

Table 4

Pre- and post-treatment difference in standard audiometric thresholds (dB) in patients with normal hearing and patients with SNHL.

Frequency kHz	Hepatitis C with normal hearing			Hepatitis C with SNHL			P
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
250 Hz	.00	.00	.00	.00	–5.00	5.00	.7
500 Hz	.00	–5.00	.00	.00	.00	5.00	.28
1000 Hz	.00	–5.00	.00	.00	.00	5.00	.11
2000 Hz	.00	.00	5.00	.00	–5.00	5.00	.87
4000 Hz	.00	.00	.00	.00	.00	5.00	.36
8000 Hz	.00	–5.00	.00	.00	–5.00	5.00	.18

P = Probability *P < .05 Test used: Mann Whitney test.

Table 5

Pre- and post-treatment differences in extended high frequency audiometric thresholds (dB) in patients with normal hearing and patients with SNHL.

Frequency Hz	Hepatitis C with normal hearing			Hepatitis C with SNHL			P
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
10 kHz	–.80	–.95	–.01	–.16	–.61	–.02	.48
12.5 kHz	–.08	–.40	.15	–.35	–1.22	.55	.8
14 kHz	.42	–.77	.83	–.17	–.59	–.02	.4
16 kHz	–.01	–.59	.52	–.16	–.58	.19	.7
18 kHz	.41	.37	.51				
20 kHz	–.10	–.59	.42				

P = Probability *P < .05 Test used: Mann Whitney test.

Table 6

Pre- and post-treatment transient otoacoustic emissions (SNR dB) in patients with normal hearing and patients with SNHL.

Frequency kHz	Hepatitis C with normal hearing				Hepatitis C with SNHL			
	Before treatment		After treatment		Before treatment		After treatment	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
1.00–7.10	6.20	2.40–12.20	6.40	2.40–10.00	8.70	5.00–13.00	11.00	1
6.00–11.40	7.40	3.30–12.00	7.0	7.00–14.00	8.70	4.00–19.00	6.00	1.5
2.00–10.60	7.00	3.20–12.00	8.80	8.00–10.90	8.70	4.10–13.00	11.10	2
3.00–9.00	4.50	3.00–7.10	4.00	5.00–11.00	9.00	5.30–12.00	8.00	3
3.40–8.00	5.90	4.00–8.20	6.40	6.50–8.00	7.00	5.80–9.00	7.00	4
4.00–8.60	6.60	4.00–11.00	6.50	6.00–11.00	8.00	6.00–13.00	7.50	1.2–3.4

IQR = interquartile range.

Table 7

Pre- and post-treatment distortion product otoacoustic emissions (SNR dB) in patients with normal hearing and patients with SNHL.

F2 frequency Hz	Hepatitis C with normal hearing				Hepatitis C with SNHL			
	Before treatment		After treatment		Before treatment		After treatment	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
750	9.00	8.00–12.00	8.80	6.10–8.80	8.90	5.00–12.00	6.10	4.10–8.00
984	10.00	8.90–11.00	9.90	8.00–11.00	7.60	6.00–10.60	6.20	3.00–12.00
1500	10.50	8.00–16.40	11.00	9.00–12.00	9.00	4.70–10.50	10.00	6.00–11.00
2016	9.60	8.00–11.00	10.10	9.00–17.70	8.20	6.60–12.00	8.00	7.00–17.00
3000	11.40	9.10–22.00	13.00	11.00–23.00	10.00	7.00–22.00	13.00	9.00–20.00
3984	10.20	9.00–16.00	9.50	9.00–11.00	9.50	8.00–11.00	8.90	7.00–11.00
6000	11.00	8.00–13.00	12.00	9.00–13.00	9.00	7.00–12.00	9.00	7.00–12.00
7969	9.00	8.00–13.00	9.00	8.00–11.00	7.00	3.00–10.10	7.80	6.00–8.50

IQR = interquartile range.

1998; Guneri et al., 2001). Some studies have suggested the possibility of early detection of hearing loss by testing evoked otoacoustic emissions (EOAE) (Sulaiman et al., 2014). Emissions are a strong indication of normal or close to normal cochlear function, and EOAEs are thus an important test of objective assessment. EOAE tests can detect changes in outer hair cell functions before any changes in standard audiometry (Baradamfar et al., 2012). In the current study, pre and post-treatment TEOAEs and DPOAEs showed no significant difference in study neither group, suggesting no

adverse effects on outer hair cells from the combination therapy of sofosbuvir and ribavirin.

A possible explanation is that sofosbuvir is a direct-acting antiviral drug that directly targets the HCV genome, impairing its ability to make copies of itself in the liver. Sofosbuvir attaches itself to the HCV RNA to block the virus from multiplying. In contrast, previously used drugs such as interferons may impair cochlear functions through various mechanisms, including autoimmune mechanisms, microvascular etiology, and/or direct ototoxic effects

Table 8

Pre- and post-treatment difference in transient otoacoustic emissions (dB) in patients with normal hearing and patients with SNHL.

Frequency kHz	Hepatitis C with normal hearing			Hepatitis C with SNHL			P
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
1	-2.10	-3.00	.40	-1.00	-2.00	.40	.5
1.5	1.00	-4.30	4.10	.70	-4.10	3.20	.8
2	-.20	-4.00	1.00	-2.00	-3.80	2.20	.6
3	-1.00	-2.10	1.10	.10	-1.00	1.00	.6
4	.30	-.10	1.20	.00	-3.20	1.50	.6
1.2–3.4	-1.00	-2.00	1.50	-1.00	-3.00	.00	.5

P = Probability *P < .05 Test used: Mann Whitney test.

Table 9

Pre- and post-treatment difference in distortion product otoacoustic emissions (dB) in patients with normal hearing and patients with SNHL.

F2 frequency Hz	Hepatitis C with normal hearing			Hepatitis C with SNHL			P
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
750	-3.00	-3.90	.00	-3.00	-5.00	-.80	.76
984	-1.10	-4.00	2.00	-3.40	-5.00	3.30	.66
1500	-.90	-5.10	1.10	.80	-4.50	2.30	.36
2016	2.90	.90	6.80	1.10	-.70	7.00	.4
3000	1.60	.00	2.00	1.00	.10	2.10	.85
3984	-1.00	-7.00	.90	-1.90	-4.50	1.00	.7
6000	1.00	-3.00	2.00	.00	-1.40	1.90	.9
7969	.40	-.80	1.00	.00	-1.00	1.70	1.00

P = Probability *P < .05 Test used: Mann Whitney test.

(Formann et al., 2004; Tunca et al., 2004).

Until now, there are no widely accepted IHC function tests readily available to clinicians, although tests sensitive to IHC dysfunction may have significant diagnostic values in assessing cochlear functional impairment and differential diagnosis between central and peripheral hearing loss, especially in cases of disproportionately poor hearing in noise (Lobarinas et al., 2016). Auditory brainstem responses (ABR), wave I amplitude in particular, can be used as a sensitive indicator of IHC deafferentation (Wynne et al., 2013). Electrocochleography (ECOG) can be used to display wave I more prominently than in ABRs (Spoendlin and Baumgartner, 1977) and to reveal potential damage to inner hair cells or afferent dysfunction. The TEN (HL) test is used to recognize cochlear dead regions (Moore et al., 2000) which may be devoid of functional inner hair cells. The previous described tests can be useful, but their limitation is that the relationship between moderate IHC loss and functional deficits requires additional study (Lobarinas et al., 2016). Lobarinas et al. (2016) concluded that IHC dysfunction and/or loss due to carboplatin increased thresholds in noise, even though this is typically associated with OHC dysfunction only. It is plausible and likely that hearing loss results from measurable loss of OHC and damages to IHC or afferent fibers. The authors recommend assessment of hearing-in-noise as a routine clinical test for evaluation of overall hearing ability and identification of hidden hearing deficits.

In recent decades, standard audiometry, extended high-frequency audiometry and otoacoustic emissions have been applied in monitoring cochlear toxicity, either separately or in combination (Lopes et al., 2009). Combination of electrocochleography, high-frequency audiometry and word recognition tasks can recognize the earliest signs of noise damage to hair cells and neurons, neither of which may not be registered by standard audiometry (Lieberman et al., 2016).

Based on previous studies, the present study was designed to evaluate auditory functions by using a combination of standard audiometry, extended high-frequency audiometry and otoacoustic emissions. Although we did not evaluate speech in noise, none of our patients reported a history of speech discrimination difficulties

in a noisy situation. This may roughly be considered as an indication of no impairment of inner hair cells. However, we hope to initiate a new study on a larger group of chronic hepatitis C patients by combining electrocochleography and or ABR, high-frequency audiometry, speech in noise tests and otoacoustic emissions.

8. Conclusion

In the current study, therapy with sofosbuvir and ribavirin in patients with chronic hepatitis C had no noticeable effects on cochlear functions. None of the patients in this study developed vertigo suggestive of vestibular impairment. Further studies are recommended to evaluate the safety of these drugs on auditory and vestibular systems in a larger group of chronic hepatitis C patients to support our findings.

Conflicts of interest

All the authors declare that they have not any conflict of interest.

Author contribution

Elshahat Ibrahim Ismail: Clinical data collection, analysis and writing of the paper.

Ashraf Elsayed Morgan: Clinical data collection, analysis and writing of the paper.

Raghda Elsayed Farag: Clinical data collection, analysis and writing of the paper.

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