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INDICATORS OF SUBJECTIVE AUDIOMETRY IN THE EXTENDED FREQUENCY RANGE IN PATIENTS WITH COVID-19

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It is known that sensorineural deafness is a polyetiological disease, and quite often, the cause of its occurrence can be inflammation, intoxication, viral and bacterial infections. As a result of the COVID-19 pandemic, a significant number of patients encountered various clinical manifestations of the disease, including lesions of the auditory analyser [3, 10, 19, 20, 22] and neurological manifestations [2, 13, 14, 23, 24, 27-29]. The share of persons in whom hearing disorders and tinnitus may be associated with the transferred COVID-19 is, respectively, ~3% and ~5% among all cases of this infectious disease [23]. According to some data, hearing impairment against the background of COVID-19 affects the high-frequency region of the acoustic spectrum [9, 26]. It may also be caused by the ototoxic side effects of drugs used to treat COVID-19 [10, 11, 12, 16, 26] or even using some protective respirators [1]. All this actualizes detailed studies of the condition of the auditory analyser against the background of COVID-19 and the development of optimal diagnostic and treatment algorithms for this pathology segment.

The study aims to assess the state of auditory function based on subjective audiometry data in an extended frequency range in patients with COVID-19.

Materials and methods

An analysis of subjective audiometry data was conducted on 32 patients with COVID-19 who complained of hearing impairment after the disease. The examination was conducted with audiometers AS-40 ("Interacoustics", Denmark). The methods of mathematical variational statistics were used using licensed software (STATISTICA v.13.3) according to generally accepted recommendations to analyse the obtained results. The average statistical value of indicators – (M) and its error (*m) were calculated. The reliability of the obtained results was assessed by the Student's t-test.

Results and their discussion

In patients who fell ill with COVID-19 and complained of hearing loss, we performed an examination of auditory function by the method of subjective audiometry. We mainly observed perceptual disorders of hearing func-

tion during the clinical and instrumental examination of patients who fell ill with COVID-19 and complained of deterioration of hearing function after the disease. This work considers just such cases of sensorineural disorders of auditory function. Patients complained of tinnitus, ear congestion, decreased hearing acuity, poor tolerance to loud sounds, unpleasant sensations in the ears (feeling of pressure, tingling, dull pain), and deterioration of speech intelligibility.

Most patients did not notice signs of impaired hearing during the disease with COVID-19 but noted that such manifestations occurred later, after complete recovery, gradually progressing. According to the data of subjective audiometry in patients with COVID-19 with sensorineural disorders of auditory function, in most cases, we observed a gently descending type of tonal audiometric curve with the most significant increase in hearing thresholds for tones in the area of high frequencies of the conventional range and disorders in the high-frequency zone. These data are published in our previous work [28].

Here is an example of a typical audiogram of a patient with sensorineural deafness after COVID-19 (Fig. 1).

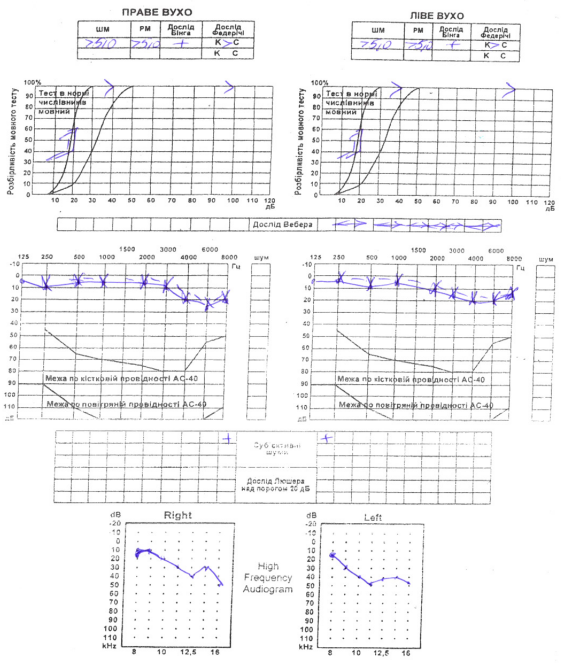

Fig. 1. Data of subjective audiometry in a patient after COVID-19.

Analysis of hearing threshold data for tones of an extended frequency range in those patients who were found to have perceptual impairment of auditory function according to subjective audiometry showed the following.

According to the values of quantitative indicators of tonal audiometry, there was a significant ($p<0.01$) increase in hearing thresholds to tones of the entire studied frequency range in the examined patients with COVID-19 compared to the individuals of the control group. The average statistics of thresholds of auditory sensitivity to tones of the extended range of the extended frequency range in the patients examined by us are shown in Table.

As can be seen from the data presented in the table, in patients with COVID-19, there is a significant ($p<0.01$) increase in hearing thresholds to tones of the entire studied range compared to controls. The most pronounced increase was at frequencies of 12, 14 and 16 kHz, with 57.6±2.3, 59.2±2.4 and 61.2±2.1 dB, respectively.

These data are more clearly presented in Fig. 2.

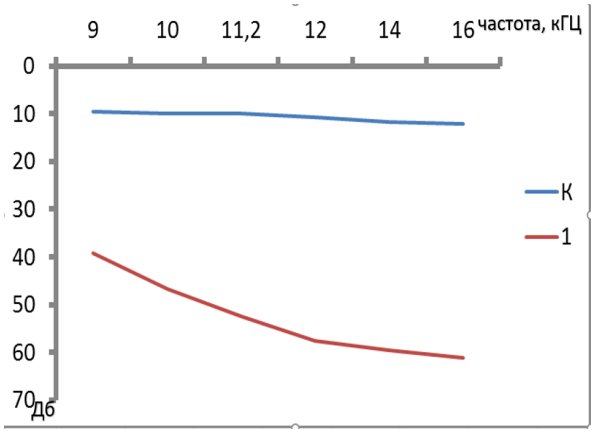

Fig. 2. Average statistical indicators of hearing thresholds for tones of the extended frequency range in patients with COVID-19 and persons in the control group (dB).

It should be noted that in some of the patients with COVID-19, who complain of a decrease in hearing function, we did not detect any violations according to the data of subjective audiometry in the conventional range, but only a

decrease in hearing sensitivity in the zone of the extended frequency range. In addition, in 12 patients who did not complain of disturbances from the auditory system, we found an increase in hearing thresholds to tones in the 9-16 kHz zone. Such patients were not included in the study presented in our work, and the detected violations require further analysis.

Average statistical indicators of hearing perception for tones of an extended frequency range in patients with COVID-19 and persons in the control group (dB)

Groups of patients	Frequency, kHz					
	9	10	11,2	12	14	16
K	9,6±0,8	9,9±0,7	9,9±0,8	10,7±0,7	11,8±0,8	12,1±1,0
1	39,3±1,9	46,8±2,3	52,5±2,2	57,6±2,3	59,5±2,4	61,2±2,1
t/p (K-1)	15,12 P<0,01	15,35 P<0,01	18,2 P<0,01	19,51 P<0,01	18,86 P<0,01	21,11 P<0,01

The data we received confirm the conclusions of many research groups regarding the probability of developing auditory function disorders in the form of perceptual disturbances in the case of COVID-19 [3, 9, 10, 23]. In addition, the results of our study are consistent with the data, which indicate the prevalence of hearing impairment in this viral pathology at the level of high-frequency noise [9, 26].

As possible pathophysiological mechanisms of hearing impairment against the background of COVID-19, disorders of microcirculation and hemoperfusion of the cochlea are considered [34], for example, thrombotic genesis [6], damage to neurons of the central or peripheral part of the auditory analyser [34], including the efferent, olivocochlear link [15] and, of course, direct viral damage to the cellular elements of the organ of Corti [7]. With a high probability, COVID-19 can directly affect the hair cells of the organ of Corti [6] since at least human vestibular hair cells are characterized by the expression of the receptor protein ACE2 (angiotensin-converting enzyme 2) for the COVID-19 virus, as well as two cofactors, TMPRSS2 (transmembrane protease serine 2) and Furin, necessary for the penetration of viral particles into the cell [18]. Direct infection of vestibular hair cells with the COVID-19 virus on explants of the human inner ear has also been described [18], as well as ACE2 expression by some hair cells of the mouse organ of Corti [31]. Also, an increase in the concentration of the protein Prestin, a key element of the mechanism of amplification of auditory perception by outer hair cells [4], is detected in blood plasma against the background of COVID-19 [30]. However, this protein is also expressed in human cardiomyocytes [33], and COVID-19 can directly cause the death of these cells [32]. In addition, for some reason, lower levels of prestin in serum are characteristic of individuals with a higher level of exposure to acoustic noise [25]. It should also be noted that the immunologically triggered role of the endocannabinoid system [5], the molecular elements of which [5, 17], as well as the usual elements of the immune system [21], are detected among the structures of the receptor apparatus of the inner ear in the pathogenesis of tinnitus after the transfer of COVID-19. Finally, the assumptions regarding the impact of COVID-19 on the central auditory analyser [8, 15, 34] still need strong direct evidence; the considered mechanisms of such influence are similar to those listed above [34] and, in our opinion, as the final link may include necrotic, autophagic or apoptotic death of neurons [7, 34]. Apparently, a similar list of mechanisms of cell death is also characteristic of damage to the hair cells of the organ of Corti against the background of COVID-19, which – In case of confirmation – will mean the possibility of a

time-differentiated manifestation of the ototoxic effects of COVID-19. Elucidation of this issue requires further thorough research.

In this regard, in our opinion, when examining patients after suffering from COVID-19, it is advisable to conduct an instrumental examination of those who have complaints of impaired hearing function and, if possible, a hearing examination in an extended frequency range.

Conclusions:

1. With COVID-19, auditory function disorders occur due to damage to the auditory system, which, in many cases in the early stages of development, can only be detected with the help of subjective audiometry in an extended frequency range.

2. The most pronounced reliable ($p<0.01$) increase in hearing thresholds to tones of an extended frequency range in patients with COVID-19 with complaints of hearing impairment compared to the control occurs at frequencies of 14 and 16 kHz, where the values in the subjects were 57, 6±2.3 and 61.2±2.1 dB, respectively.

4. For patients with COVID-19 who complain of auditory dysfunction, it is advisable to conduct an instrumental audiological examination, particularly tonal threshold audiometry in an extended frequency range, to detect early signs of sensorineural deafness.

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A b s t r a c t

It is known that, quite often, the cause of sensorineural deafness can be inflammation, intoxication, and viral and bacterial infections. As a result of the COVID-19 pandemic, many patients encountered various clinical manifestations of the disease, including damage to the auditory analyser. It actualizes detailed studies of the condition of the auditory analyser against the background of COVID-19 and the development of optimal diagnostic and treatment algorithms.

The study aims to assess the state of auditory function based on subjective audiometry data in an extended frequency range in patients with COVID-19.

Materials and methods: An analysis of subjective audiometry data was conducted on 32 patients with COVID-19 who complained of hearing impairment after the disease. The examination was conducted with audiometers AS-40 ("Interacoustics", Denmark).

Results and their discussion: By clinical and instrumental methods, we examined patients who became ill with COVID-19 and complained of deterioration of auditory function after the disease. We observed perceptual disorders of auditory function. Patients complained of tinnitus, ear congestion, decreased hearing acuity, poor tolerance to loud sounds, unpleasant sensations in the ears (feeling of pressure, tingling, dull pain), and deterioration of speech intelligibility.

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The analysis of data on hearing thresholds for tones of an extended frequency range based on subjective audiometry data in patients with COVID-19 with perceptual disorders of auditory function showed that there was a significant ($p<0.01$) increase in hearing thresholds for tones of the entire studied population compared to the control range The most pronounced such increase was at frequencies of 12, 14 and 16 kHz, where the values were 57.6±2.3, 59.2±2.4 and 61.2±2.1 dB, respectively.

Conclusions:

1. With COVID-19, auditory function disorders occur due to damage to the auditory system, which, in many cases in the early stages of development, can only be detected with the help of subjective audiometry in an extended frequency range.

2. The most pronounced reliable ($p<0.01$) increase in hearing thresholds to tones of an extended frequency range in patients with COVID-19 with complaints of hearing impairment compared to the control occurs at frequencies of 14 and 16 kHz, where the values in the subjects were 57.6±2.3 and 61.2±2.1 dB, respectively.

3. For patients with COVID-19 who complain of auditory dysfunction, it is advisable to conduct an instrumental audiological examination, particularly tonal threshold audiometry in an extended frequency range, to detect early signs of sensorineural deafness.

Key words: COVID-19, auditory function, perceptual hearing disorders, sensorineural deafness, subjective audiometry, hair cell apoptosis.

ПОКАЗНИКИ СУБ'ЄКТИВНОЇ АУДІОМЕТРІЇ У РОЗШИРЕНОМУ ДІАПАЗОНІ ЧАСТОТ У ХВОРИХ НА COVID-19

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А н о т а ц і я

Відомо, що досить часто причиною виникнення сенсоневральної приглухуватості можуть бути запалення, інтоксикації, вірусні та бактеріальні інфекції. Внаслідок пандемії COVID-19 значна кількість хворих зіткнулися з різноманітними клінічними проявами захворювання, у тому числі з ураженнями слухового аналізатора. Це актуалізує детальні дослідження стану слухового аналізатора на тлі COVID-19 і розробку оптимальних діагностичних та лікувальних алгоритмів.

Мета дослідження: оцінка стану слухової функції за даними суб'єктивної аудіометрії у розширеному діапазоні частот у хворих на COVID-19.

Матеріали і методи: Проведено аналіз даних суб'єктивної аудіометрії у 32 хворих на COVID-19, які скаржилися на погіршення слухової функції після захворювання. Обстеження проводилося за допомогою аудіометрів АС-40, («Interacoustics», Данія).

Результати та їх обговорення: При обстеженні клінічними та інструментальними методами пацієнтів, які перехворіли на COVID-19 та скаржилися на погіршення слухової функції після захворювання, ми спостерігали перцептивні порушення слухової функції. Пацієнти скаржилися на шум у вухах, закладеність вух, зниження гостроти слуху, погану переносимість гучних звуків, неприємні відчуття у вухах (відчуття тиску, поколювання, тупий біль), погіршення розбірливості мови.

Більшість хворих не відмічали ознаки порушень слухової функції під час захворювання на COVID-19, а зазначали, що такі прояви мали місце згодом, після повного одужання, поступово прогресуючи. За даними суб'єктивної аудіометрії у хворих на COVID-19 з сенсоневральними порушеннями слухової функції в більшості випадків ми спостерігали пологонизхідний тип тональної аудіометричної кривої з найбільшим підвищенням порогів слуху на тони у області високих частот конвенціонального діапазоні і порушеннями у високочастотній зоні.

Аналіз даних порогів слуху на тони розширеного діапазону частот за даними суб'єктивної аудіометрії у хворих на COVID-19 з перцептивними порушеннями слухової функції показав, що у них спостерігається достовірне ($p<0,01$) порівняно з контролем підвищення порогів слуху до тонів усього досліджуваного діапазону. Найбільш вираженим таке підвищення було на частотах 12; 14 та 16 кГц, де значення становили 57,6±2,3; 59,2±2,4 та 61,2±2,1 дБ, відповідно.

Висновки:

1. При COVID-19 мають місце порушення слухової функції внаслідок ураження слухової системи, які в багатьох випадках на ранніх стадіях розвитку можуть бути виявлені лише за допомогою суб'єктивної аудіометрії у розширеному діапазоні частот.

2. Найбільш виражене достовірне ($p<0,01$) порівняно з контролем підвищення порогів слуху до тонів розширеного діапазону частот у хворих на COVID-19 зі скаргами на порушення слуху має місце на частотах 14 та 16 кГц, де значення у досліджуваних склали 57,6±2,3 та 61,2±2,1 дБ, відповідно.

3. Хворим на COVID-19, які пред'являють скарги на порушення слухової функції, доцільно проводити інструментальне аудіологічне обстеження, зокрема тональну порогову аудіометрію у розширеному діапазоні частот з метою виявлення ранніх ознак сенсоневральної приглухуватості.

Ключові слова: COVID-19, слухова функція, перцептивні порушення слуху, сенсоневральна приглухуватість, суб'єктивна аудіометрія, апоптоз волоскових клітин.