Salud, Ciencia y Tecnología. 2024; 4:.575
doi: 10.56294/saludcyt2024.575

ORIGINAL

Combined effects of alcohol and lead on cerebrospinal fluid production

Efectos combinados del alcohol y el plomo en la producción de líquido cefalorraquídeo

Gamal Ashirbekov[1], Uldana Alsherieva[2], Kyralai Ashirbekova[3], Tokhzhan Narymbetova[4], Nurlan Khodzhayev[5]

[1]Department of Pathological Anatomy, Forensic Medicine with the Course of Pathological Physiology, Kazakh-Russian Medical University. Almaty, Republic of Kazakhstan.
[2]Department of Pathological Anatomy with the Course of Forensic Medicine, Asfendiyarov Kazakh National Medical University. Almaty, Republic of Kazakhstan.
[3]Department of Therapy, Asfendiyarov Kazakh National Medical University. Almaty, Republic of Kazakhstan.
[4]Department of Human Morphology and Physiology, Khoja Akhmet Yassawi International Kazakh-Turkish University. Turkestan, Republic of Kazakhstan.
[5]Department of Pathology, Khoja Akhmet Yassawi International Kazakh-Turkish University. Turkestan, Republic of Kazakhstan.

Cite as: Ashirbekov G, Alsherieva U, Ashirbekova K, Narymbetova T, Khodzhayev N. Combined effects of alcohol and lead on cerebrospinal fluid production. Salud, Ciencia y Tecnología. 2024; 4:.575. https://doi.org/10.56294/saludcyt2024.575

Submitted: 12-02-2024 **Revised:** 21-05-2024 **Accepted:** 17-09-2024 **Published:** 18-09-2024

Editor: Dr. William Castillo-González

Corresponding author: Gamal Ashirbekov[1]

ABSTRACT

Currently, due to the development of industry, a high incidence of heavy metal salt poisoning is observed, especially in people with alcohol dependence. The study aims to investigate the combined effects of these pathogens on the central nervous system. The study demonstrates changes in intracranial pressure and cerebrospinal fluid production in isolated and combined poisoning of lead and ethanol based on experimental models on 10 and 40 days of exposure, 3 main groups were formed – the group of lead salts, ethanol, combined intoxication, after which the main indicators were measured. The effect of separate and combined action of alcohol and lead on cerebrospinal fluid production and haemodynamic indices in experimental animals was studied. It was found at 40-day intoxication indices remained above normal, systemic arterial pressure was 131,8 mmHg, and the rate of cerebrospinal fluid production was 0,073±0,002 ml/min. Combined 10-day combined action of alcohol and lead enhances their excitatory effect, which is characterised by an increase in systemic arterial pressure (to the level of 135,6 mmHg) and general psycho-somatic agitation, the rate of cerebrospinal fluid production was 0,077±0,008 ml/min. The 40-day co-exposure manifested mainly toxic effects of lead, as shown by a decrease in cerebrospinal fluid production of 0,049±0,001 ml/min, and a decrease in blood pressure to a level of 93,6 mmHg. The results of this study will make it possible to develop treatment protocols for patients with ethanol and heavy metal salt poisoning, especially in the field of anti-oedema therapy.

Keywords: Intracranial Pressure; Liquor; Neurology; Poisoning; Ethanol; Intoxication.

RESUMEN

En la actualidad, debido al desarrollo de la industria, se observa una elevada incidencia de intoxicaciones por sales de metales pesados, especialmente en personas con dependencia del alcohol. El estudio pretende investigar los efectos combinados de estos patógenos en el sistema nervioso central. El estudio demuestra los cambios en la presión intracraneal y la producción de líquido cefalorraquídeo en la intoxicación aislada y combinada de plomo y etanol sobre la base de modelos experimentales en 10 y 40 días de exposición, se

formaron 3 grupos principales - el grupo de sales de plomo, etanol, intoxicación combinada, después de lo cual se midieron los principales indicadores. Se estudió el efecto de la acción separada y combinada de alcohol y plomo sobre la producción de líquido cefalorraquídeo y los índices hemodinámicos en animales de experimentación. Se comprobó que a los 40 días de intoxicación los índices se mantenían por encima de lo normal, la presión arterial sistémica era de 131,8 mmHg y la tasa de producción de líquido cefalorraquídeo era de 0,073±0,002 ml/min. La acción combinada de 10 días de alcohol y plomo potencia su efecto excitatorio, que se caracteriza por un aumento de la presión arterial sistémica (hasta el nivel de 135,6 mmHg) y agitación psicosomática general, la tasa de producción de líquido cefalorraquídeo fue de 0,077±0,008 ml/min. La coexposición de 40 días manifestó principalmente efectos tóxicos del plomo, como lo demuestra una disminución de la producción de líquido cefalorraquídeo de 0,049±0,001 ml/min, y una disminución de la presión arterial hasta un nivel de 93,6 mmHg. Los resultados de este estudio permitirán elaborar protocolos de tratamiento para pacientes con intoxicación por etanol y sales de metales pesados, especialmente en el ámbito de la terapia antiedematosa.

Palabras clave: Presión intracraneal; Licor; Neurología; Envenenamiento; Etanol; Intoxicación.

INTRODUCTION

Alcohol and lead, two common neurotoxins, have devastating effects on the central nervous system (CNS), causing serious biological and psychological changes in the human body. These substances have come under increasing scrutiny and analysis in light of their adverse effects on health and social well-being. Alcohol, as one of the most widely used psychoactive substances in the world, has a strong association with a multitude of social and health problems. According to Sabyrova and Molchanov[1] the number of people who used alcohol increased to 35,7 %. According to Aitbaeva et al.[2], about 80 % of all fatalities due to exogenous poisoning in the Republic of Kazakhstan are attributed to alcohol poisoning.

Lead, in turn, is another toxic agent that can significantly impair human health. It can be sourced from contaminated water, soil, and the uncontrolled use of lead-based materials in industry and construction. This metal may be accumulated in the body, which leads to chronic poisoning, and also hurts the CNS. There is also data given by Battakova and Saipov[3], that the maximum number of cases of heavy metal poisoning is the zone of central Kazakhstan, where the main mining and metallurgical enterprises of the country are concentrated, as well as according to Cherednichenko et al.[4], the norms of heavy metals in the air in these regions exceeds the norm several times. In addition, the concentration of heavy metals in the hair and blood plasma of the population decreases with increasing distance from industrial centres.[5]

It is known that when ingested, they can cause a variety of brain dysfunctions leading to severe organic lesions such as alcoholic neuropathy, atrophy of the prefrontal cortex, decreased grey matter density of the brain, and the development of oedema. According to Adams and Perry[6], ethanol intake increases the concentration of markers of neural tissue damage in cerebrospinal fluid in humans. In all of the above studies, direct measurement of cerebrospinal fluid production was not performed due to the impossibility of safely performing this procedure. Their combined action is particularly dangerous since the combined effect of toxicants can significantly increase their negative effects. One of the important indicators of the state of the central nervous system is the production of cerebrospinal fluid (CSF), which is closely related to cerebral haemodynamics, as well as the composition can determine the main markers of neural tissue damage.[7]

The study aims to investigate the combined poisoning of lead and ethanol salts on the nervous tissue of the brain by assessing the dynamics of CSF reproduction, which serves as an indirect indicator of the viability of cells in the nervous system.

METHOD

The study was carried out on sexually mature mongrel dogs of both sexes, with body weight from 9 to 15 kg, under modelling of acute and chronic poisoning. Preliminary animals were kept in the vivarium, and before the beginning of the experiment were kept in quarantine for 12-14 days. The dogs were kept in normal conditions of the vivarium at a temperature of 18-25°C, received standard food, and were taken into the experiment on an empty stomach.

An experimental study of haemodynamics and the rate of cerebrospinal fluid production in mongrel dogs was carried out, both in isolated lead and alcohol poisoning and in combination. Four groups were created: an experimental group, a group to which acetic acid lead was orally administered, a group intoxicated with 30 % alcohol and the last group – to which alcohol and acetic acid lead were administered together, the 4th group of animals controlled. Lead intoxication in animals was induced by oral administration of a 5 % solution of lead acetic acid at a dose of 50 mg/kg body weight for 10 and 40 days. The degree of intoxication was judged by

the general condition and behaviour of the animals, as well as by the character of haemo- and liquorodynamic parameters. Alcohol intoxication was also induced by oral administration of 30 % alcohol solution at a dose of 3 ml/kg body weight, during the same period as lead poisoning. In combined poisoning, lead and alcohol solutions were administered in the same doses and by the same route.

Before the study and examination of haemodynamics and cerebrospinal fluid production rate, the animals were injected intramuscularly with hexenal anaesthesia. In dogs under hexenal anaesthesia (30-40 mg/kg), a midline incision of the skin and musculotendinous helmet of the head from the coronal suture to the occipital tubercle was made. The muscles of the cranial vault were detached, the periosteum was peeled off with a raspater, and then milling holes were made in the skull according to the projections of the sagittal sinus and one of the lateral ventricles of the brain. After stopping the haemorrhage, all the investigated biological objects of the head were punctured and connected to pressure sensors and a device for recording the volumetric production of CSF using flexible transmitters. The animals were brought to the state of clinical death and all traumatic manipulations were performed under hexenal anaesthesia, as pain sensitivity was depressed and myorelaxation occurred. After the experiment, experimental animals were killed simultaneously with control animals by administering a high dose of anaesthesia. Ethical standards were strictly observed when working with animals.

Systemic arterial and venous pressures were measured by cannulation of the carotid artery and jugular vein with a T-shaped cannula. Heparin (10 mg/kg body weight) was injected into the latter to prevent blood clotting. The pressure in the sagittal sinus was monitored immediately after its puncture through the cutter hole. To determine the rate of CSF production, the level of liquor pressure by moving the mobile node was set to 10-15 mmHg lower than the pressure in the sagittal sinus. In this case, resorption was stopped, and newly formed CSF came out through the puncture needle and increased the level of fluid in the pressure chamber, as a result of which excess fluid in the form of drops constantly flowed out through the tube. As the droplet fell, it closed the contacts on the capacitor sensor. This signal was fed through a stabilised power supply unit to a “drop marker” (1 drop=0,06 ml) mounted on the polyphysiograph. After counting the rate of CSF formation, pressure levels in the craniospinal cavity, in particular, the liquor pressure in the great cerebral cistern, were determined after a suboccipital puncture. The studied pressure indices from the subarachnoid cavity were brought to the registration channel of the polyphysiograph. Each indicator was measured for 3-5 minutes. The first channel recorded blood pressure in the carotid artery. The second channel – liquor pressure in the large cistern of the brain. The third channel – venous pressure in the sagittal sinus. The fourth – in the jugular vein. The fifth channel recorded the volumetric rate of CSF production. The results of production determination obtained by this method and perfusion methods in humans were mostly similar and were 0,2-0,7 ml/min.

The obtained digital material was subjected to statistical processing, where the reliability of differences between arithmetic averages was established by Student’s criterion with the determination of the probability of difference – P. The difference was considered statistically significant at $p<0,05$. A comparative analysis was also performed, including synthesis (combining the results of different stages of the study) and analysis (obtaining data on the 10th and 40th day of the study, studying the effect of different toxins on the production of cerebrospinal fluid when administered alone and in combination).

RESULTS

After 10-day lead poisoning, no special changes were observed in the general condition and behaviour of the animals. Compared to control animals, in experimental animals with 10-day lead acetic acid poisoning, the rate of CSF production was slightly lower and was 0,053±0,003 ml/min (0,064±0,009 ml/min in controls). Arterial pressure in animals poisoned for 10 days was slightly elevated compared to control animals and was 128,7±3,2 mmHg, systemic venous pressure (PV) in jugular veins did not differ significantly from control data and was 40,9±2,1 mmHg. Furthermore, in comparison with control animals in animals with 10-day lead poisoning, the values of venous pressure in sinuses of dura mater were slightly increased – 111,7±6,3 mmHg (in the control group – 90,7 mmHg).

Animals with 40-day lead intoxication practically all initially demonstrated decreased haemodynamic parameters. Changes in the initial haemodynamic indices may indicate abnormalities in cardiac and vascular function in animals under lead exposure. These changes may be related to the toxic effects of lead on the cardiovascular system, such as deterioration of cardiac contractile function, reduction of vascular tone or changes in blood vessels, as well as to toxic effects on the regulatory centres of the cardiovascular system in the medulla oblongata. Arterial was 83,7±4,2 mmHg, and systemic BP in the jugular veins was 35,6±1,1 mmHg. Venous pressure in the sinuses of the dura mater was 80,9±5,6 mmHg (90,7 mmHg in the control group). Almost all experimental animals showed a decrease in the rate of CSF production. The dynamics of the rate of CSF production increase remained the same as in the case of poisoning for 10 days and reached 0,058 ml/min, with a low initial value (0,042+0,002 ml/min). Systemic arterial pressure was 131,8 mmHg, and the rate of cerebrospinal fluid production was 0,073±0,002 ml/min.

https://doi.org/10.56294/saludcyt2024.575

After 10 days of lead poisoning, the animals showed no obvious changes in general condition and behaviour and generally remained active and well-fed. However, changes in haemodynamic parameters were observed. Decreased cerebrospinal fluid production rate and increased arterial and venous pressure indicate possible dysfunctions in the cerebrospinal fluid system and blood circulation during short-term lead exposure. Animals with 40-day lead intoxication showed decreased arterial and venous pressures and decreased cerebrospinal fluid production rates. These changes may indicate deeper disturbances in the functioning of organs and systems of the organism during long-term lead exposure.

Firstly, the study showed that animals injected with alcohol had a marked increase in mean arterial pressure (MAP) to an average of 142,9 mmHg, which was significantly higher than in the control group, where this index was 112,3 mmHg. This indicates that alcohol has a significant effect on the cardiovascular system, leading to an increase in BP. Second, sagittal sinus pressure (SSP) was also significantly increased and reached 107,6±5,1 mmHg, while in controls this index was at 90,7 mmHg. This indicates the effect of alcohol on blood circulation in the brain and may relate to the negative effects of alcohol on brain activity. Third, the systemic BP in the jugular veins was relatively stable and did not differ significantly from the control data, being 40,9±2,1 mm a.v. This may indicate that the venous system of the body is less sensitive to the effects of alcohol in this context. Fourthly, the study of CSF production rate revealed a marked increase in this index, almost 1,5-fold, compared to the control group, reaching 0,092±0,006 ml/min, while in controls this index was 0,06 ml/min. This indicates changes in the cerebrospinal fluid under the influence of alcohol and may be relevant to its effects on the brain and central nervous system.

Furthermore, it is important to note that animals injected with alcohol for 40 days showed a decrease in systemic MAP and CSF production rate compared to the group injected with alcohol only for 10 days. This may indicate the presence of adaptation of the organism to the effects of alcohol during its prolonged use. It is also important to emphasise that a systematic regular procedure was performed in the animals during alcohol intoxication, and this may be important for understanding the effects of alcohol that occur with regular consumption. In addition, the observation of habituation to alcohol in animals, which was detected when it was consumed for a prolonged period of 40 days, emphasises the importance of studying the dependence and long-term effects of alcohol consumption. The depressive state and symptoms observed during the experiment are indicative of organic damage to the nervous tissue.

The results of the haemo- and liquorodynamics study showed that the combined effect of lead and alcohol for 10 days caused an increase in BP, and its level was slightly higher than in experiments with separate poisoning with alcohol and lead. Venous pressure in the sinuses of the cerebral dura mater increased to almost the same values as in animals with lead poisoning for 10 days. The rate of CSF production in combined poisoning with lead and alcohol was markedly lower than in the experiments with alcohol, but in comparison with the data obtained in experimental animals with 10-day lead poisoning, it was slightly higher. Systemic arterial pressure was 135,6 mm. Hg, general psychosomatic agitation, and the rate of cerebrospinal fluid production was 0,077±0,008 ml/min. Thus, it is possible to conclude that 10-day combined poisoning with lead and alcohol is manifested by mutual potentiation of their excitatory action, i.e., promotes a more vivid manifestation of the first stage of toxic agent exposure.

The experimental animals subjected to combined poisoning with alcohol and lead for 40 days showed the same changes in their general condition as animals with 40-day lead poisoning. In particular, the animals became lethargic, apathetic, and indifferent to external stimuli. Appetite was absent in many. Animals lost up to 25 % of their original weight. Many had vomiting and diarrhoea. Several experimental dogs had liquid stools with blood. Muscle twitching in the limbs, especially in the hind limbs, was noted in 75 % of the animals. Two dogs died of intoxication before the end of the experiment. This experimental group of animals had a more severe condition than the group where poisoning was carried out with only 5 % solution of acetic acid lead for 40 days. Comparative analysis of haemodynamics and changes in CSF production in animals poisoned with lead and alcohol for 40 days with the data of separate poisoning with these substances shows that changes in BP, DSS and BP in combined poisoning more resemble the parameters of animals with 40-day lead intoxication and differ markedly from the results obtained in 40-day alcohol poisoning (CSF production rate – 0,049±0,001 ml/min, blood pressure – 93,6 mmHg).

The experimental results obtained in this series indicate that alcohol in moderate doses and on its own is rarely the cause of convulsive syndromes since there are no significant metabolic disturbances and the mechanisms of regulation of cerebral circulation are preserved. In turn, prolonged combined intoxication with alcohol and lead causes impaired autoregulation of cerebral blood flow, which does not provide sufficient cerebral perfusion, especially with changes in intracranial pressure.

DISCUSSION

Studies of haemo- and liquorodynamics showed that the sympathetic nervous system plays an important role in the regulation of cerebrospinal fluid production. The sympathetic nervous system controls a variety

of physiological processes, including the regulation of blood pressure and blood flow.[8] In this context, it influences the process of cerebrospinal fluid production. Moderate irritation of the sympathetic nervous system can have an inhibitory effect on cerebrospinal fluid production. This means that when the sympathetic nervous system is moderately stimulated, there is a decrease in the volume of cerebrospinal fluid produced by the body.

Lead intoxication also affects haemo- and liquorodynamics. Mild lead intoxication may cause an increase in arterial and venous pressures, while severe intoxication may cause a decrease.[9, 10] Lead causes dysfunction of dopaminergic, cholinergic, and glutamatergic signalling pathways in nerve transmission, which impairs the cardiovascular centre in the medulla oblongata. Alcohol consumption can cause an increase in vascular tone, leading to an increase in blood pressure.[11] This effect is due to vasoconstriction, in which blood vessels constrict, leading to increased pressure in the circulatory system. In the initial stages of alcohol consumption, there is an increase in the rate of CSF production.[12]

In the combined effect of alcohol and lead, there are differences from the changes caused by the isolated action of these substances. Short-term exposure (10 days) to alcohol and lead has a mutual enhancement of their excitatory effects on the haemo- and liquorodynamic system, but on day 40 all manifestations correlate with the lead poisoning group, suggesting that alcohol does not affect the severity of lead salt poisoning.[13, 14]

According to Togao et al.[15], lead is predominantly accumulated in the hippocampus, thalamus in the hypothalamus, the kidneys, in the liver, which characterises the clinical picture of poisoning by this metal. In our study in laboratory animals on the 40th day of lead exposure there were convulsions, decreased appetite, weight loss, decreased blood pressure and decreased rate of cerebrospinal fluid formation, which is a sign of central nervous system, kidney, and liver parenchyma damage. Bai et al.[16] found that lead inhibits autophagy of lead-affected proteins and thus accumulates in tissues. Chen et al.[17] proved that lead increases the membrane permeability of nerve tissue cells, which is reflected in the decreased production of cerebrospinal fluid. In addition, lead salts induce anti-myelin proteolytic activity, which is also reflected in fluid retention in nervous tissue, through the development of moderate oedema.[18] In addition, the teratogenic properties of lead on the nervous tissue of the forming foetus are known, which is manifested in low cognitive abilities, as well as in disorders of neuroplasticity, and neuromuscular transmission, as reflected by Meyer et al.[19]

De la Monte and Kril[20] highlight several mechanisms of the ethanol effect on the nervous tissue, including microcirculation disturbance, disruption of neuronal and oligodendrocyte function and metabolism, and impaired formation of new synapses. Nutt et al.[21] studied in detail the molecular mechanisms of neurotoxicity of ethanol on nervous tissue, among which it is worth noting the lack of thiamine, the neurotoxic effect of products of ethanol metabolism (acetaldehyde), neuroinflammation due to inhibition of NMDA-receptors. Behl et al.[22] also note the role of disruption of the synaptic membrane due to disruption of NMDA-receptors, but in addition, they note that ethanol causes oxidative stress in neurons by reducing the level of antioxidants and generation of free radicals. However, these mechanisms work only with prolonged consumption of alcoholic beverages. Visontay et al.[23] found a correlation between long-term alcohol consumption and increased risk of dementia in old age. Similarly, Peng et al.[24] found an increased risk of Parkinson's disease with long-term alcohol consumption. In this study, similar results were obtained, on the 10th day of ethanol intake psychomotor excitement was observed, and an increase in liquor production due to the stimulating effect, but on the 40th day of ethanol intake apathy developed, the rate of cerebrospinal fluid production decreased, which may indicate damage to nervous tissue due to increased membrane permeability of white and grey matter cells, which is manifested by fluid retention in brain tissue.

According to Rangel-Barajas et al.,[25] intoxication with lead salts causes an increased risk of developing ethanol dependence, due to the mechanism of dysregulation of glutamate transporter 1 (GLT1) and glutamate/cystine antiporter (xCT). Albrecht et al.[26] came to the same conclusions but described a different mechanism, due to an increase in the stimulatory effect of ethanol in lead poisoning, which is associated with a decrease in the rate of ethanol metabolism in nervous tissue. In the course of the experiment, the development of ethanol dependence in laboratory animals was also noted, but no difference in the rate of development of this complication was noted, which may indicate a low effect of lead on the development of alcohol dependence in laboratory animals, but it is necessary to conduct additional experiments in this area.

Thus, the combined effect of alcohol and lead on cerebrospinal fluid production is manifested by mutual potentiation of their excitatory action on the system of haemo- and liquorodynamics, especially in the first stage of poisoning. However, as the duration of poisoning increases, the effects become similar to those of severe lead intoxication, indicating the predominant role of lead in this process.

CONCLUSIONS

The study highlights the significant neurotoxic effects of lead salts and ethanol intoxication on the human body. Lead exposure leads to early signs of neurotoxicity such as altered cerebrospinal fluid dynamics and increased blood pressure, which worsen with prolonged exposure, causing severe multi-organ toxicity. Ethanol initially increases cerebrospinal fluid production but can lead to neurotoxicity over time, especially when

combined with lead, enhancing their psychostimulant effects. Prolonged combined exposure exacerbates neurotoxic symptoms, including seizures, underscoring the heightened risk compared to individual exposures. These findings underscore the critical need for caution in occupational and lifestyle settings to mitigate the severe health risks associated with lead and ethanol exposure. Further research is warranted to develop effective diagnostic protocols for early lead intoxication detection and to better understand long-term effects of combined exposure to ethanol and lead salts.

REFERENCES

1. Sabyrova M, Molchanov SN. Comparative analysis of approaches to the treatment of alcohol dependence in the use and in Republic of Kazakhstan. German Int J Modern Sci. 2021;18:38-40. DOI: 10.24412/2701-8369-2021-18-38-40.

2. Aitbaeva GM, Dzharkimbekova GK, Akhmetov FW, Kamalov GT. Analysis of mortality in acute exogenous poisoning in Almaty division of toxicology in 17 years. Bull Kazakh Nat Med Univ. 2015;4:383-5.

3. Battakova K, Saipov A. Geography of population diseases in industrial cities of central Republic of Kazakhstan. Sci Eur. 2022;100:21-6. DOI: 10.5281/zenodo.7049675.

4. Cherednichenko VS, Cherednichenko AV, Cherednichenko AV, Zheksenbaeva AK, Madibekov AS. Heavy metal deposition through precipitation in Kazakhstan. Heliyon. 2921;7(1):e05844. DOI: 10.1016/j.heliyon.2020.e05844.

5. Batyrova G, Tlegenova Z, Kononets V, et al. Hair toxic trace elements of residents across the Caspian oil and gas region of Kazakhstan: Cross-sectional study. J Environ Res Public Health. 2022;19(18):11158. DOI: 10.3390/ijerph191811158.

6. Adams C, Perry N, Conigrave J, et al. Central markers of neuroinflammation in alcohol use disorder: A meta-analysis of neuroimaging, cerebral spinal fluid, and postmortem studies. Alcohol Clin Exp Res. 2023;47(2):197-208. DOI: 10.1111/acer.14992.

7. Hnatjuk M, Nesteruk S, Tatarchuk L, Monastyrska N. Morphometric assessment of age-related structural changes in the vessels of the microcirculatory bed of the prostate gland under conditions of ethanol intoxication. Bull Med Biol Res. 2023;17(3):8-15. DOI: 10.61751/bmbr.2706-6290.2023.3.8.

8. Ilderbayev O, Okassova A, Rakhyzhanova S, Ilderbayeva G, Zhazykbayeva L. The levels of oxidative stress in a combination of stress factors. J Med Life. 2022;15(8):927-31. DOI: 10.25122/jml-2021-0060.

9. Lukyanenko N, Lenha E, Spaska A, Klets T, Shevchenko T. Tactics for treating young children with pyelonephritis and vesicoureteral reflux associated with impaired fibrillogenesis. Mol Cell Biochem. 2023;478(3):531-8. DOI: 10.1007/s11010-022-04529-7.

10. Tamm TI, Datsenko BM, Nepomniashchiĭ VV, et al. Diagnostics and tactics of treatment in patients with acute pancreatitis complicated by jaundice syndrome. Klin Khirur. 2009;7-8:122-3.

11. Belov SG, Tamm TI, Mamontov IN, Nepomnyashchiy VV. Perforation of peptic ulcer: Nonstandard situations and nonstandard decisions. Klin Khirur. 2016;3:69–72.

12. Messina A, Concerto C, Rodolico A, Petralia A, Caraci F, Signorelli MS. Is it time for a paradigm shift in the treatment of schizophrenia? The use of inflammation-reducing and neuroprotective drugs – A review. Brain Sci. 2023;13(6):957. DOI: 10.3390/brainsci13060957.

13. Komar TV, Khmara TV, Tsyhykalo OV, Hrechko DI, Khmara AB. Features of the blood supply of some areas of the head in human fetuses. Bull Med Biol Res. 2023;15(1):10-4. DOI: 10.11603/bmbr.2706-6290.2023.1.13337.

14. Hasiuk OP. Pharmacological and morphological features and socioeconomic aspects of cannabidiol: A literature review. Int J Med Med Res. 2023;9(1):47-59. DOI: 10.61751/ijmmr.2413-6077.2023.1.47.

15. Togao M, Nakayama SMM, Ikenaka Y, et al. Bioimaging of Pb and STIM1 in mice liver, kidney and brain using Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS) and immunohistochemistry.

Chemosphere. 2020;238:124581. DOI: 10.1016/j.chemosphere.2019.124581.

16. Bai L, Wu Y, Wang R, et al. Prepubertal exposure to Pb alters autophagy in the brain of aging mice: A time-series based model. Brain Res Bull. 2022;189:22-33. DOI: 10.1016/j.brainresbull.2022.08.013.

17. Chen L, Liu Y, Jia P, et al. Acute lead acetate induces neurotoxicity through decreased synaptic plasticity-related protein expression and disordered dendritic formation in nerve cells. Environ Sci Pollut Res. 2022;29(39),58927-35. DOI: 10.1007/s11356-022-20051-1.

18. Latronico T, Fasano A, Fanelli M, et al. Lead exposure of rats during and after pregnancy induces anti-myelin proteolytic activity: A potential mechanism for lead-induced neurotoxicity. Toxicology. 2022;472:153179. DOI: 10.1016/j.tox.2022.153179.

19. Meyer DN, Crofts EJ, Akemann C, et al. Developmental exposure to Pb2+ induces transgenerational changes to zebrafish brain transcriptome. Chemosphere. 2020;244:125527. DOI: 10.1016/j.chemosphere.2019.125527.

20. de la Monte SM, Kril JJ. Human alcohol-related neuropathology. Acta Neuropathol. 2014;127:71-90. DOI: 10.1007/s00401-013-1233-3.

21. Nutt D, Hayes A, Fonville L, et al. Alcohol and the Brain. Nutrients. 2021;13(11):3938. DOI: 10.3390/nu13113938.

22. Behl T, Yadav HN, Sharma PL. Alcoholic neuropathy: Involvement of multifaceted signalling mechanisms. Cur Mol Pharmacol. 2021;14(1):2-10. DOI: 10.2174/1874467213666200512114943.

23. Visontay R, Rao RT, Mewton L. Alcohol use and dementia: New research directions. Cur Opinion Psych. 2021;34(2):165-70. DOI: 10.1097/yco.0000000000000679.

24. Peng B, Yang Q, Joshi RB, et al. Role of alcohol drinking in Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Int J Mol Sci. 2020;21(7):2316. DOI: 10.3390/ijms21072316.

25. Rangel-Barajas C, Coronel I, Zhang Y, Hernández M, & Boehm II SL. Low-level developmental lead exposure does not predispose to adult alcohol self-administration, but does increase the risk of relapsing to alcohol seeking in mice: Contrasting role of GLT1 and xCT brain expression. Neuropharmacology. 2020;181:108339. DOI: 10.1016/j.neuropharm.2020.108339.

26. Albrecht PA, Fernandez-Hubeid LE, Deza-Ponzio R, Virgolini MB. The intertwining between lead and ethanol in the model organism Caenorhabditis elegans. Front Toxicol. 2022;4:991787. DOI: 10.3389/ftox.2022.991787.

27. Alvarado MAG. Gentrification and Community Development: An analysis of the main lines of research. Gentrification 2023;1:2–2. https://doi.org/10.62486/gen20232.

28. Auza-Santivañez JC, Apaza-Huanca B, Diaz-Guerrero JL, Vallejos-Rejas DRE, Zelaya-Espinoza Y, Vargas-Gallego I, et al. Relevance of ultrasound detection and assessment of vascular calcifications in chronic kidney disease. Multidisciplinar (Montevideo) 2024;2:77–77. https://doi.org/10.62486/agmu202477.

29. Ayala DP, Falero DML, Pita MM, González IC, Silva JW. Ozone therapy in periodontal disease in type 2 diabetic patients. Odontologia (Montevideo) 2024;2:120–120. https://doi.org/10.62486/agodonto2024120.

30. Benavidez AMV, Ozeta RJN, Davila CAC, Hernandez OH, Mogollon JAY. Conceptual maps using Cmap Tools and student learning at a National Intercultural University Fabiola Salazar Leguía of Bagua. Multidisciplinar (Montevideo) 2024;2:107–107. https://doi.org/10.62486/agmu2024107.

31. Cano CAG. Education, urbanism, and gentrification: convergence of issues and solutions. Gentrification 2023;1:1–1. https://doi.org/10.62486/gen20231.

32. Cardozo GT. Community development promoted by policies: an analysis from the perspective of gentrification. Gentrification 2023;1:3–3. https://doi.org/10.62486/gen20233.

33. Dinkar AK, Haque MA, Choudhary AK. Enhancing IoT Data Analysis with Machine Learning: A Comprehensive Overview. LatIA 2024;2:9–9. https://doi.org/10.62486/latia20249.

34. Espinoza GYG. Transforming the Salitre campus into a smart campus: proposal of smart initiatives for the Gerardo Barrios University of El Salvador. LatIA 2024;2:102–102. https://doi.org/10.62486/latia2024102.

35. Galván LNO, Ayala DP, Lozano IM, Falero DML, Silva JW. Breastfeeding, Oral Habits, and Malocclusions in Children Aged 3 to 6 Years. Odontologia (Montevideo) 2024;2:101–101. https://odonto.ageditor.uy/index.php/odonto/article/view/101

36. García EA, Curbelo ML, Iglesias MSS, Falero DML, Silva JW. Oral lesions associated with the use and care of dentures in the elderly. Odontologia (Montevideo) 2024;2:100–100. https://doi.org/10.62486/agodonto2024100.

37. González MS, Pérez AG. Proposal of actions to improve accessibility at the Hotel Las Yagrumas, Artemisa. Management (Montevideo) 2024;2:25–25. https://doi.org/10.62486/agma202425.

38. Hernández-Lugo M de la C. Artificial Intelligence as a tool for analysis in Social Sciences: methods and applications. LatIA 2024;2:11–11. https://doi.org/10.62486/latia202411.

39. Iyengar MS, Venkatesh R. A Brief Report on Building Customer Loyalty in Luxury hotels: A Universal Approach. Management (Montevideo) 2024;2:32–32. https://doi.org/10.62486/agma202432.

40. Iyengar MS, Venkatesh R. Customer preferences while booking accommodation in hotels: Customer Behaviour and Hotel Strategies. Management (Montevideo) 2024;2:31–31. https://doi.org/10.62486/agma202431.

41. León MP. The impact of gentrification policies on urban development. Gentrification 2023;1:4–4. https://doi.org/10.62486/gen20234.

42. Lozano IM, Molina YG, Santos IF, Galván LNO, Pérez AP, Becerra CEC. Behavior of Denture Stomatitis in Adults Over 45 Years of Age. Odontologia (Montevideo) 2024;2:102–102. https://doi.org/10.62486/agodonto2024102.

43. Macedo GC, Auza-Santivañez JC, Rejas DREV, Sarmiento RAQ, Canaviri JJF, Laime LHS. Giant multiloculated omental cyst in a pediatric patient. Case report and literature review. Multidisciplinar (Montevideo) 2024;2:88-88. https://doi.org/10.62486/agmu202488.

44. Martinez AME, Warnes CD. English language skills and their influence on the academic performance of high school students in the public schools of Cereté – Córdoba. Multidisciplinar (Montevideo) 2024;2:108–108. https://doi.org/10.62486/agmu2024108.

45. Ramirez GAM, Murillo MYR, Valderrama PJC, Patiño ML, Mora YJR. Analysis of the strategic plan for the Acuña Ventures SAS company in Yopal city, Colombia. Management (Montevideo) 2024;2:29–29. https://doi.org/10.62486/agma202429.

46. Sonal D, Mishra K, Haque A, Uddin F. A Practical Approach to Increase Crop Production Using Wireless Sensor Technology. LatIA 2024;2:10–10. https://doi.org/10.62486/latia202410.

47. Vargas OLT, Agredo IAR. Active packaging technology: cassava starch/orange essential oil for antimicrobial food packaging. Multidisciplinar (Montevideo) 2024;2:102–102. https://doi.org/10.62486/agmu2024102.

48. Du X, Zheng W, Ye Q. Rare cases of severe life-threatening lead poisoning due to accident or chronic occupational exposure to lead and manganese: Diagnosis, treatment, and prognosis. Toxicol Indust Health. 2020;36(12):951-9. DOI: 10.1177/0748233720958969.

FINANCING

The authors did not receive financing for the development of this research.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

Conceptualization: Gamal Ashirbekov, Uldana Alsherieva.
Research: Kyralai Ashirbekova.
Methodology: Tokhzhan Narymbetova.
Project management: Gamal Ashirbekov.
Resources: Tokhzhan Narymbetova, Nurlan Khodzhayev.
Supervision: Gamal Ashirbekov.
Validation: Uldana Alsherieva, Nurlan Khodzhayev.
Drafting - original draft: Gamal Ashirbekov, Uldana Alsherieva, Kyralai Ashirbekova, Tokhzhan Narymbetova, Nurlan Khodzhayev.
Writing - proofreading and editing: Gamal Ashirbekov, Uldana Alsherieva, Kyralai Ashirbekova, Tokhzhan Narymbetova, Nurlan Khodzhayev.

https://doi.org/10.56294/saludcyt2024.575