GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 9 (294) Сентябрь 2019

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

МЕДИЦИНСКИЕ НОВОСТИ ГРУЗИИ

Ежемесячный совместный грузино-американский научный электронно-печатный журнал
Агентства медицинской информации Ассоциации деловой прессы Грузии,
Академии медицинских наук Грузии, Международной академии наук, индустрии,
образования и искусств США.
Издается с 1994 г., распространяется в СНГ, ЕС и США

Website:
www.geomednews.org

The International Academy of Sciences, Education, Industry & Arts. P.O.Box 390177,
Mountain View, CA, 94039-0177, USA. Tel/Fax: (650) 967-4733

Версия: печатная. **Цена:** свободная.
Условия подписки: подписка принимается на 6 и 12 месяцев.
По вопросам подписки обращаться по тел.: 293 66 78.
Контактный адрес: Грузия, 0177, Тбилиси, ул. Асатиани 7, III этаж, комната 313
тел.: 995(32) 254 24 91, 995(32) 222 54 18, 995(32) 253 70 58
Fax: +995(32) 253 70 58, e-mail: ninomikaber@hotmail.com; nikopir@dgmholding.com

По вопросам размещения рекламы обращаться по тел.: 5(99) 97 95 93

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press; Georgian Academy of Medical Sciences; International Academy of Sciences, Education, Industry and Arts (USA).

Published since 1994. Distributed in NIS, EU and USA.

CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 3th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 222-54-18
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

WEBSITE

www.geomednews.org

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

რეზიუმე

ჭრილობის არხის მაკროფაგოციტების ულტრასტრუქტურის ცვლილებების დინამიკა ცეცხლნასროლი დაზიანების შემდეგ

[1]რ. მიხაილუსოვი, [2]ვ. ნეგოდუიკო, [3]ვ. ნევზოროვი, [3]ო. ნევზოროვა, [1]ტ. დენისიუკი

[1]ხარკოვის დიპლომისშემდგომი განათლების სამედიცინო აკადემია; [2]უკრაინის თავდაცვის სამინისტროს ჩრდილოეთის რეგიონის სამხედრო-სამედიცინო კლინიკური ცენტრი; [3]ვ. ზაიცევის სახ. ზოგადი და გადაუდებელი ქირურგიის ინსტიტუტი, უკრაინა

კვლევის მიზანს წარმოადგენდა ჩონჩხის კუნთების სუბმიკროსკოპული არქიტექტონიკის გადაწყობის თავისებურების, ორგანელებისა და უჯრედშიდა მემბრანების ტრანსფორმაციის დინამიკის განსაზღვრა ცეცხლნასროლი ნამსხვრევი ჭრილობის მოდელირების სხვადასხვა ვადაზე.

დაკვირვების ქვეშ იყო 26 ბოცვერი, რომელთაც ჭრილობა მიაყენეს პისტოლეტიდან "ფორტი-12". ბოცვერები ექსპერიმენტიდან გამოჰყავდათ დაზიანებიდან 30-ე და მე-60 დღეს. ულტრასტრუქტურული ანათლები, ტყვიის ციტრატით კონტრასტირების შემდგომ, შეისწავლებოდა ელექტრონული მიკროსკოპით ЭМ-125 (სუმი, უკრაინა) ამაჩქარებელი ძაბვით 75 კვ, გადიდებით 42000-72000.

ჭრილობის არხის ნაწიბუროვანი ქსოვილიდან აღებული მაკროფაგოციტების ორგანელების ელექტრონულ-მიკროსკოპიული კვლევით ჭრილობის მიყენებიდან 30-ე დღეს გამოვლინდა მაღალი ფუნქციური აქტივობის მდგომარეობაში მყოფი მაკროფაგოციტების უხვი რაოდენობა, ორგანელების დისტროფიული და დესტრუქციული ცვლილებები ბირთვის მემბრანების, მიტოქონდრიების და გრანულური ენდოპლაზმური რეტიკულუმის კეროვანი დაზიანებებით. კატაბოლური პროცესების მიმდინარეობა გამოწვეული იყო ტოქსიკური კომპონენტების, დაშლილი მიოსიმპლასტების და დამაზიანებელი ელემენტის მძიმე მეტალების იონების არსებობით ჭრილობის არხში. დაზიანებიდან მე-60 დღეს შენარჩუნებული იყო მაკროფაგოციტების მომატებული აქტივობა, გამოწვეული მიოსიმპლასტების დაზიანებული ულტრასტრუქტურული კომპონენტების და დამაზიანებელი ელემენტის მძიმე მეტალების იონების უტილიზაციის დუნედ მიმდინარე პროცესებით.

MANAGEMENT OF AMNESTIC AND BEHAVIORAL DISORDERS AFTER KETAMINE ANESTHESIA

[1]Belenichev I., [2]Burlaka B., [4]Puzyrenko A., [5]Ryzhenko O., [3]Kurochkin M., [4]Yusuf J.

Zaporozhye State Medical University, [1]Department of Pharmacology and Medical Recipe; [2]Department of Drug Technology; [3]Department of Pediatrics; [4]All Saints University School of Medicine, Department of Pharmacology, Roseau, Dominica; [5]ICU, 5th Children's Hospital, Zaporizhzhia, Ukraine

General anesthesia may cause damage of the central nervous system and cognitive dysfunction in the postoperative period. The frequency of postoperative cognitive dysfunction – 36,8% [1,2]. The early postoperative cognitive dysfunction is the main predictor of the stable amnestic disorder. It makes worse the patient's quality of life [3-5]. Neuroprotective drugs have an important role in preventing the neuron damage and cognitive dysfunction at the early postoperative period when these changes are potentially reversible [1,2,6-7]. The neuroprotective drugs have a direct influence on memory and mental activity and also increase steadiness of brain to the aggressive effect of hypoxia, injuries, intoxication [2]. A new intranasal form of Noopept (N-Phenylacetyl-L-prolylglycine ethyl ester) was developed by our team at the Department of the medical technology (Zaporizhzhia State Medical University, Ukraine). This work aimed to estimate the neuroprotective action of Noopept and to prove using in the clinic for correction of amnestic and behavioral disorders after ketamine anesthesia.

Material and methods. All experimental studies were conducted in accordance with the "Methodological recommendations for conducting preclinical studies of potential drugs of the State Expert Center of the Ministry of Health of Ukraine". The studies were performed on a sufficient number of experimental animals. All manipulations were carried out according to the regulation of using of the animals in biomedical experiments (Strasbourg 1986, as amended in 1998). The protocols of experimental studies were approved by the decision of the Ethical Committee of the Zaporizhzhia State Medical University (protocol No. 77 of Aprile 5th, 2018).

50 mature male Wistar-Kyoto rats with body weight of 200-220g were treated in a common laboratory environment (12-hour light cycle, T=+22°C) with free access to water and food. All rats were 6 months old. Animals were obtained from the Institute of Pharmacology and Toxicology of the Academy of Medical Sciences of Ukraine. The duration of the quarantine (acclimatization period) for all animals was 14 days. During the quarantine, every animal was inspected daily (behavior and general condition). Before the beginning of the study, animals that met the criteria for inclusion in the experiment were divided into groups by using the randomization method. Animals that did not meet the criteria were excluded from the study during the quarantine. Cells with animals were placed in the separate rooms.

Ketamine anesthesia was made by the intraperitoneal administration of 100mg/kg ketamine. After recovery from anesthesia the single administration of the drugs in following doses was made: 10mg/kg Noopept by the intranasal way, 0,2mg/kg

cerebrocurin intraperitoneally, 250mg/kg piracetam intraperitoneally. The intact group (the animals without administration of ketamine) received 1ml/100g normal saline intraperitoneally once, and the control group (the animals after ketamine anesthesia) received 1ml/100g normal saline intraperitoneally once. The next day after anesthesia the estimation of motor and search activity by the open field test and in the labyrinth was made during the next 10 days.

Cerebrocurin (Scientific Production Enterprise, Ukraine) is a white, slightly yellowish transparent liquid with pH 6,1-6,4. It contains neuropeptides, including proteins S-100, reelin, nerve growth factor, amino acids [12,13].

Piracetam was used in the form of 20% solution (Arterium, Ukraine).

Noopept (OTCpharm, Russia) is a homogeneous transparent liquid without odor with the low viscosity in the nasal form (Patent # 126979, Ukraine).

Determination of motor activity

Determination of motor activity was carried out by the open field test using arena 80x80x35cm. The animal was placed in the center of the area, and then it has been allowed to walk across the arena freely for 8 min. We estimated general walked distance, general motor activity, structure of activity (high, low activity, torpidity), quantity of freezing and entering in center, distance walked near wall, vertical search activity (quantity of rearing near wall and free standing), quantity of short and long grooming events, quantity of defecation and urination.

Estimation of reference and working memory

Investigations of memory were carried out with radial labyrinth LE760 (AgnTho's, Sweden). Radial arm maze consists of an octagonal platform (lateral length 22cm) with outgoing 8 radial ray-paths 70cm length and 10cm wide. Each path is closed by the guillotine mechanism independently of one another. All installation was placed at the height of 70cm from the floor. The investigation was carried out in silence.

Starting from the first day animals were placed in the central part with 4 closed rays and 4 opened rays. 200mg of food was put into troughs. Combination of opened and closed rays was individual and regular for each animal. Each animal was trained in food search using visual landmark for 10 min. The experiment was repeated every day twice for each animal. The animals have gotten daily food ration after the experiments. On the 10th day, the animal was placed in a radial labyrinth with 8 opened ray-paths, and in 4 of ray-paths the food was put according to habitual scheme for the individual animal. We estimated the number of referent memory mistakes (first visit the earlier closed ray where animal never found the food), and the number of working memory mistakes (repeated visit the ray where animal found or not found food earlier). Besides, we estimated traversed distance and general motor activity.

Table. Influence of noopept, cerebrocurin and piracetam on rat's behavioral activity and memory after ketamine anesthesia

Index	Intact group	Control group	Ketamine anesthesia+ Cerebrocurin	Ketamine anesthesia+ Piracetam	Ketamine anesthesia+ Noopept
Radial labyrinth					
Number of referent memory mistakes	2	3	2	3	$1^{\#,\dagger}$
Number of working memory mistakes	4±1	$13±1^{*}$	$5±1^{\#,\dagger}$	$12±1^{*}$	$2^{\#,\&,\dagger}$
General motor activity, cm^2/s	24380,98±124,4	26867,58±154,5	$44862,35±168,5^{*,\#,\dagger}$	27552,12±123,1	$34863,66±108,5^{*,\#,\&,\dagger}$
Open field					
Traveled distance, cm	4161,82±29,78	4202,03±77,1	$3094,16±34,5^{*,\#,\dagger}$	4013,25±42,36	3916,56±24,48
Number of entering to centre, unit	1	2	1±1	2	1
High activity, %	7,83±1,44	$14,83±2,07^{*}$	$21,83±1,58^{*,\#,\dagger}$	$12,22±1,21^{*}$	$10,50±1,45^{\#,\&}$
Low activity, %	61,71±7,08	65,83±4,03	65,17±3,69	66,22±7,44	$78,30±1,59^{*,\#,\&,\dagger}$
Torpidity, %	30,47±6,59	22,34±4,37	13,00±4,64	21,22±5,11	$11,20±3,67^{*,\#}$
Immobility, unit	284±35	$429±27^{*}$	$85±21^{*,\#,\dagger}$	$434±33^{*}$	$138±17^{*,\#,\dagger}$
Freezing, unit	284±35	$529±27^{*}$	$374±32^{*,\#,\dagger}$	$539±21^{*}$	$242±28^{\#,\&,\dagger}$
Free distance, cm	59,37±26,31	$529,76±21,98^{*}$	$323,64±88,71^{*,\#,\dagger}$	$612,12±55,43^{*,\#}$	$226,10±33,44^{*,\#,\dagger}$
Free distance, %	1,43±0,61	$11,30±2,67^{*}$	$8,92±2,01^{*}$	$12,74±2,0^{*}$	$6,06±1,20^{*,\#,\dagger}$
Distance near wall, cm	4102,44±289,55	3672,27±312,74	$2770,53±281,43^{*,\#,\dagger}$	3700,82±332,90	3690,16±110,34
Standing near wall, unit	4±1	$8±1^{*}$	$5±1^{\#}$	$7±1^{*}$	$5±1^{\#}$
Free standing, unit	2	2±1	1	1±1	1±1
Short grooming, unit	4	2^{*}	3	$2±1^{*}$	3
Long grooming, unit	1	1	1	1	1
Defecation, unit	3	2	2±1	2	1
Urination, unit	1±1	1	1	1	2

notice: * - p<0.05 vs Intact group; $^{\#}$ - p<0.05 vs Control group; $^{\&}$ - p<0.05 vs Cerebrocurin group; † - p<0.05 vs Piracetam group

Data obtaining and handling

Investigations were carried out at the department of experimental pathophysiology and functional morphology of the Training medico-laboratory center (Zaporizhzhia State Medical University, Ukraine). Experiments have been performed in a well-illuminated room in silence. During the test, the influence of external and internal visual, olfactory and auditory stimuli was excluded. Evaluation of animal's behavior was carried out by the technician without knowledge about belonging animal to the concrete experimental group. Capture and image recording were made by using the color-video camera SSC-DC378P (Sony, Japan). Analysis of video file was made by using software Smartv 3.0 (Harvard Apparatus, USA). All statistical calculations were done by «STATISTICA® for Windows». A significant difference was considered at $p<0.05$.

Results and their discussion. Evaluation of the specific indexes of open field test showed the negative influence of ketamine anesthesia on the animal behavior (Table). Administration of ketamine didn't lead to a valid change of traveled distance but increased the free distance. In the control group, the rising number of the freezing and immobility of the animals were observed. All these factors indicate a forming of anxiety and excitability of the animals after ketamine anesthesia. Administration of ketamine didn't change a number of free-standing of the animals but led to increasing of standing near the wall in 2 times. Also, the number of short grooming acts was decreased and a number of long grooming was invariable. This fact also indicates a forming of anxiety and excitability of the animals after ketamine anesthesia. Rising of high activity also may be estimated as decreasing of ability to search because a rat makes a lot of unnecessary movements and needs more time for learning a new environment.

When specific training indexes in radial labyrinth were carried out it was revealed that in 10 days after ketamine anesthesia the cognitive dysfunction of animals was present. General activity of animals in the control group hadn't valid differences with intact group. It was established that on the 10 days after administration of ketamine the number of working memory mistakes was increased in 3 times what indicates a breach of amnestic function after ketamine anesthesia.

Obtained data relate to the conception of the postoperative cognitive dysfunction due to ketamine which can lead to forming the stable cognitive deficit and also psycho-emotional disorders – lethargy, fear, anxiety, disorientation, aggressiveness, irritability [14,15]. Administration of ketamine may provoke deposition of amyloid beta-protein and so can provoke long-term cognitive effects [16]. Other reasons for cognitive dysfunction due to ketamine are considered (e.g. inhibition of glutamate transmission, exhaustion of energetic balance and circulatory ischemia) [17].

Our study showed increased free distance in 10 times compare to the intact group after piracetam administration. Piracetam didn't reduce the number of freezing and torpidity. A number of standing near the wall in the piracetam group stayed high and unchanged compare to control group. A number of short grooming acts was at the level of the control group as well. These facts indicate that piracetam doesn't decrease anxiety, fear, excitability and uncomfortable state of the animals after ketamine anesthesia. Also, piracetam didn't have a positive influence on the indexes of cognitive-amnestic functions. The number of mistakes of working and referent memory was not decreased.

Administration of cerebrocurin after ketamine anesthesia reduced anxiety and excitability. So cerebrocurin reduced free distance, number of freezing and standing near the wall. At the same time, the cerebrocurin didn't have an influence on the animal's comfortability (grooming) and led to rising of high activity compare to intact and even compare with a control group. Cerebrocurin significantly decreased the number of mistakes of working memory and referent memory on the 10th day after ketamine anesthesia.

Protective effects of cerebrocurin on the brain tissue may include its action on the energetic metabolism and homeostasis of calcium, intracellular protein synthesis [2]. Effects of cerebrocurin can have a connection with increasing of neuron plasticity [9].

Intranasal administration of noopept to the animals after ketamine anesthesia led to reducing of anxiety, fear, excitability and had a good effect on emotional status and behavior of the animals. Noopept reduced free distance, a number of standing near wall and immobility compare to control group. Noopept decreased the high (unproductive) activity and increased the low activity.

Noopept significantly reduced the number of working memory mistakes after ketamine anesthesia, and also it was the best result among other investigated compounds. Intranasal administration of noopept also decreased the number of referent memory mistakes. These facts show the high antiamnesic effect of noopept after ketamine anesthesia and significant neuroprotective effect.

Noopept has an antioxidant action by reducing oxidative destruction of the protein molecules including memory proteins and also by decreasing accumulation of nitrosative stress markers. So noopept can prevent the neuron destruction [18]. Neuroprotective action of noopept may have a connection with the level of anti-inflammatory interleukins [8-11,18-19].

Conclusions.

1. Ketamine anesthesia leads to increasing of anxiety, excitability and worsening of search activity and leads to amnestic dysfunction.
2. Parenteral administration of piracetam doesn't have a significant influence on the animal's behavior, excitability and doesn't have an effect on the animal's memory after ketamine anesthesia.
3. Parenteral administration of cerebrocurin lowers anxiety and also shows some antiamnesic effect.
4. Intranasal administration of noopept after ketamine anesthesia significantly decreases anxiety and excitability, raises the animal's activity, shows an intensive antiamnesic effects and increases animal's training ability. Noopept significantly exceeds piracetam and cerebrocurin according to neuroprotective effects.

REFERENCES

1. Belenichev IF, Chernij VI, Nagornaya EA, Pavlov SV. Neuroprotection and neuroplasticity. Kiev: Logos; 2015.
2. Belenichev IF, Chernij VI, Kolesnik UM. Rational neuroprotection. Donetsk; 2009.
3. Bolshedvorov RV, Kichin VV, Fedorov SA, Lichvantsev VV. Epidemiology of postoperative cognitive disorders. Anesthesia and reanimation. 2009; 3: 20-23.
4. Fodale V, Santaria LB, Schifilliti D, Mandel PK. Anesthetics and postoperative cognitive dysfunction: a pathological mechanism mimicking Alzheimer's disease. Anesthesia. 2010; 65(4): 388-395.
5. Shnajder NA, Shprah VV, Salmina AB. Postoperative cognitive dysfunction (diagnostics, prevention, treatment). Krasnoyarsk; 2005.
6. Pappa M, Theodosiadis N, Tsounis A. Pathogenesis and treatment of post-operative cognitive dysfunction. Electron Physician. 2017; 9(2): 3768-3775.

7. Shnajder N. Role and place of pharmacological cerebroprotection in prevention and correction of cognitive insufficiency: hypothesis and proof. Ukrainian health. 2007; 3(160): 29-30.
8. Kligunenko EN, Dzjak LA, Ploshenko UA, et al. Neuroprotection in anesthesiology and intensive therapy. International neurologic journal. 2008; 2: 41-50.
9. Belenichev IF, Pavlov SV, Dunaev VV. Neuroprotective effect of cerebrocurin in a model of acute cerebral stroke. Eksp Klin Farmakol. 2010; 73(2): 6-9.
10. Belenichev I, Sokolik E, Abramov A. Pharmacological modulation of apoptosis signaling in neurons of cal-zone of hippocampus of rats with chronic alcohol intoxication. Innovative Journal of Medical and Health Science. 2011; 3: 12-16.
11. Zarubina IV, Shabanov PD. Neuroprotective effects of peptides during ischemic preconditioning. Bull Exp Biol Med. 2016; 160(4): 448-51.
12. Buresh Y. Methods and general experiments of brain and behavior investigation. Moscow: Medicine; 1991.
13. Gimmelfarb GN. Anesthesia of experimental animals. Tashkent: Fan; 1994.
14. Lee C, Jones TA. Effects of ketamine compared with urethane anesthesia on vestibular sensory evoked potentials and systemic physiology in mice. J Am Assoc Lab Anim Sci. 2018; 57(3): 268-277.
15. Kang JG, Lee CJ, Kim TH, et al. Analgesic effects of ketamine infusion therapy in korean patients with neuropathic pain: a 2-week, open-label, uncontrolled study. Curr Ther Res Clin Exp. 2010; 71(2): 93-104.
16. Crumb MW, Bryant C, Atkinson TJ. Emerging trends in pain medication management: back to the future a focus on ketamine. Am J Med. 2018; 343(18): 30291-2.
17. Jonkman K, Dahan A, van de Donk T, Aarts L, Niesters M, van Velzen M. Ketamine for pain. 2017; 6: 1711-3.
18.Ostrovskaia RU, Vakhitova IuV, Salimgareeva MK, et al. On the mechanism of noopept action: decrease in activity of stress-induced kinases and increase in expression of neutrophines. Eksp Klin Farmakol. 2010; 73(12): 2-5.
19. Ostrovskaia RU, Gudasheva TA, Voronina TA, Seredenin SB. The original novel nootropic and neuroprotective agent noopept. Eksp Klin Farmakol. 2002; 65(5): 66-72.

SUMMARY

MANAGEMENT OF AMNESTIC AND BEHAVIORAL DISORDERS AFTER KETAMINE ANESTHESIA

[1]Belenichev I., [2]Burlaka B., [4]Puzyrenko A., [5]Ryzhenko O., [3]Kurochkin M., [4]Yusuf J.

Zaporozhye State Medical University, [1]Department of Pharmacology and Medical Recipe; [2]Department of Drug Technology; [3]Department of Pediatrics;[4]All Saints University School of Medicine, Department of Pharmacology, Roseau, Dominica; [5]ICU, 5th Children's Hospital, Zaporizhzhia, Ukraine

General anesthesia may cause damage of the central nervous system and cognitive dysfunction in the postoperative period. A new intranasal form of Noopept (N-Phenylacetyl-L-prolylglycine ethyl ester) was developed by our team at the Department of the medical technology (Zaporizhzhia State Medical University, Ukraine).

The objectives of this investigation were the study of neuroprotective action of Noopept and to prove using in the clinic for correction of amnestic and behavioral disorders after ketamine anesthesia. We discovered that the intranasal administration of noopept after ketamine anesthesia significantly decreases anxiety and excitability, raises the animal's activity, shows an intensive antiamnesic effects and increases animal's training ability. Noopept significantly exceeds piracetam and cerebrocurin according to neuroprotective effects.

Keywords: ketamine, N-Phenylacetyl-L-prolylglycine ethyl ester, noopept, cerebrocurin, piracetam, neuroprotection.

РЕЗЮМЕ

ФАРМАКОЛОГИЧЕСКАЯ КОРРЕКЦИЯ КОГНИТИВНО-АМНЕСТИЧЕСКИХ И ПОВЕДЕНЧЕСКИХ НАРУШЕНИЙ ПОСЛЕ КЕТАМИНОВОЙ АНЕСТЕЗИИ

[1]Беленичев И.Ф., [2]Бурлака Б.С., [4]Пузыренко А.Н., [5]Рыженко О.И., [3]Курочкин М.Ю., [4]Юсуф Д.

Запорожский государственный медицинский университет, [1]кафедра фармакологии; [2]кафедра технологии лекарственных средств; [3]кафедра педиатрии; [4]Университет всех святых, кафедра фармакологии, Розо, Доминика; [5]V детская больница, реанимационное отделение, Запорожье, Украина

Общая анестезия часто вызывает повреждение центральной нервной системы и когнитивную дисфункцию в послеоперационном периоде. Новая интраназальная форма Ноопепта (этиловый эфир N-фенилацетил-L-пролилглицин) разработана сотрудниками кафедры технологии лекарственных средств Запорожского государственного медицинского университета.

Цель исследования - определение нейропротекторного действия Ноопепта и обоснование его использования в клинике для коррекции амнестических и поведенческих расстройств после кетаминового наркоза.

Обнаружено, что интраназальное введение Ноопепта после анестезии кетамином значительно снижает беспокойство и возбудимость, повышает активность животного, проявляет интенсивный антиамнестический эффект и повышает способность животного к тренировкам. Ноопепт значительно превосходит пирацетам и цереброкурин по нейропротекторному эффекту.

რეზიუმე

ამნეზიური და ქცევითი დარღვევების მართვა კეტამინური ანესთეზიის შემდეგ

[1]ი. ბელენიჩევი, [2]ბ. ბურლაკა, [4]ა. პუზირენკო, [5]ო. რიჟენკო, [3]მ. კუროჩკინი, [4]დ. იუსუფი

ზაპოროჟიეს სახელმწიფო სამედიცინო უნივერსიტეტი, [1]ფარმაკოლოგიის კათედრა; [2]სამკურნალწამლო ტექნოლოგიების კათედრა; [3]პედიატრიის კათედრა; [4]„ყოვლად წმინდას“ უნივერსიტეტი, ფარმაკოლოგიის კათედრა, როზო, დომინიკა; [5]V საბავშვო საავადმყოფო, რეანიმაციის განყოფილება,ზაპოროჟიე, უკრაინა

ზოგადმა ანესთეზიამ შეიძლება გამოიწვიოს ცენტრალური ნერვული სისტემის დაზიანება და აღქმითი დისფუნქცია პოსტოპერაციულ პერიოდში.

ნოოპეპტის (N ფენილაცეტილ-L-პროლიგლიცინ ეთილის ეთერი) ახალი ინტრანაზალური ფორმა შე-

მუშავდა სამედიცინო ტექნოლოგიების დეპარტამენტის თანამშრომლების მიერ უკრაინის ზაპოროჟიეს სახელმწიფო სამედიცინო უნივერსიტეტში. კვლევის მიზანს წარმოადგენდა ნოოპეპტის ნეიროპროტექტორული მოქმედების შესწავლა და მისი კლინიკური გამოყენების მართებულობის დამტკიცება ამნესტიური (ცნობიერებისა) და ქცევითი დარღვევებისას კეტამინის ანესთეზიის შემდეგ.

აღმოჩნდა, რომ ნოოპეპტის ინტრანაზალური მოხმარება კეტამინური ანესთეზიის შემდეგ მნიშვნელოვნად ამცირებს შფოთვას და აგზნებადობას, აძლიერებს "ცხოველურ" აქტიურობას, გამოხატავს ინტენსიურ ანტიამნეზიურ ეფექტს და ზრდის ვარჯიშის უნარს. ნეიროპროტექტორული ეფექტის მიხედვით ნოოპეპტი მნიშვნელოვნად აღემატება პირაცეტამს და ცერებროკურინს.

EVALUATION OF STRUCTURAL CHANGES IN THE AREA OF EXPERIMENTAL MANDIBULAR DEFECT WHEN APPLYING OSTEOPLASTIC MATERIALS BASED ON VARIOUS COMPONENT PERCENTAGE OF HYDROXYAPATITE AND POLYLACTIDE

[1]Skochylo O., [1]Mysula I., [2]Ohonovsky R., [2]Pohranychna Kh., [2]Pasternak Yu.

[1]Ivan Horbachevsky Ternopil State Medical University, Department of Surgical Dentistry;
[2]Danylo Halytsky Lviv National Medical University, Department of Surgical Dentistry and Maxillofacial Surgery, Ukraine

Defects in bone structures of different genesis, location and size are quite common in the practice ofdental surgeons and maxillofacial surgeons and orthopedic general practitioners, as well as general orthopedic doctors [5,12]. The only effective way to treat such clinical cases is to use a variety of bone substitutes, which can significantly adjust the processes of reparative regeneration and rehabilitation of patients with this pathology [1,2]. A large amount of scientific studies has been devoted to this issue, but the problem has not been fully resolved yet [3,4,6].

Given the significant growth in various contagious infectious diseases, transmitted between organisms regardless of their species, and certain bioethical issues, plastic materials of synthetic origin have become most prevalent [7]. A number of authors emphasize the use of materials based on analogues of the mineral component of bones, particularly hydroxyapatite. [8, 10]

Although in the scientific literature there are references and research data of such compositions, solving the problem of choice is far from complete, since there is still no universal material that would meet all necessary requirements [9]. In this regard, it is relevant to keep searching for new materials that would optimize the processes of reparative osteogenesis and studying the mechanisms of bone tissue regeneration under their influence [11].

In fact, there are few studies that would investigate and compare regenerative processes with percentage compositional variants, and no practical guidance on how to use them has been provided [13].

The main aim is to find out the mechanisms of reparative regeneration of bone tissue in artificially created transversemandibular defects in rats when applying osteoplastic materials based on hydroxyapatite and polylactide with different component percentage.

Material and methods. Experimental studies were carried out on 114 mature laboratory white male 180-220 g rats fed on a standard vivarium diet in compliance with all the requirements of the “European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes” (Strasbourg, 1986).

To perform the tasks, all animals were divided into groups (36 rats each): control group - animals whose bone defect was filled only with a blood clot; 1st experimental group - the entire defect volume was densely filled with a block with the ratio of component parts, hydroxyapatite 80% + polylactide 20%; 2nd experimental group was similar, but with the ratio of 50% + 50% [14]. There was also a separate group of intact animals (6 rats) that did not undergo intervention, but onlytheir blood samples were collected to determine the norm of biochemical parameters to be compared.

An experimental defect was created using a spherical dental 2 mm diameter bur according to the method of Chechin A.D. (1989) [15], using a Surgec XT physiodispenser (NSK, Japan) at a speed of 800 rpm constantly cooling the bur with 0.9% saline solution. Perforation defects were created through external access in the submandibular area to the left. Polylactide (PL) - Poly (L-Lactide) Purasorb PL 32 (Netherlands) and hydroxyapatite (HA) Ca10 x (PO4) 6 (OH) 2 with a particle size of 0.1mm (sintering temperature = 10500C), synthesized at the department of chemical technology of silicates at Lviv Polytechnic university, were used to create the osteo preservation composition (Fig. 1).

Fig. 1. Photo of the obtained composite material