The Pharma Innovation Journal 2018; 7(7): 461-464

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2018; 7(7): 461-464

www.thepharmajournal.com
Received: 20-05-2018
Accepted: 21-06-2018

Tetyana Khomazyuk
State Establishment "Dnipropetrovsk medical academy of Health Ministry of Ukraine

Viktoriia Krotova
State Establishment "Dnipropetrovsk medical academy of Health Ministry of Ukraine

Correspondence
Tetyana Khomazyuk
State Establishment "Dnipropetrovsk medical academy of Health Ministry of Ukraine

Early diagnosis and new approaches to treatment of cognitive impairment in patients with vascular comorbid pathology

Tetyana Khomazyuk and Viktoriia Krotova

Abstract
The article is devoted to one of the topical problems of clinical medicine – brain damage as a target organ in arterial hypertension. Particular attention is paid to cognitive impairment that arises in hypertension. The data of the neuropsychological study used in the diagnosis of cognitive impairment in hypertension are presented. The results of research on memory, attention, level of anxiety and vegetative status, quality of life and cerebrovascular reserve are considered. The role of combined effect of fenibut and ipidacrine in complex therapy of violations of cognitive functions in hypertension is shown, efficiency at this pathology is shown according to the results of clinical research, and recommendations on the practical application of fenibut and ipidacrine in clinical practice are presented.

Keywords: arterial hypertension, cognitive impairment, fenibut, ipidacrine

Introduction
The greatest part in the structure of the causes of mortality is the disease of the circulatory system, which predominates the frequency of tumors in 6,5 times. The results of large-scale clinical studies allow us to conclude that age, hypertension, multifocal atherosclerosis and cognitive function (CF) are interrelated, affect the level of disability, the development of dementia, quality of life and social maladaptation [25, 27, 30, 31, 38]. According to WHO data on cardiovascular disease (CVD) 17.5 million people die, but one of the most common diseases blood circulation is arterial hypertension (AH), at which the risk of developing CVD increases 3-fold. As you know, hypertension is a major risk factor for stroke and chronic cerebrovascular disorders [7, 20, 36]. In the majority of patients with long-term AH, high blood pressure (BP) does not always cause severe circulatory disorders, which are accompanied by clinical manifestations. With an increase in blood pressure, blood flow is decreased not only in the system of main general carotid arteries, but also internally in the cerebral arteries. Spasm of the peripheral arteries with elevated blood pressure leads to ischemia, local small focus lesions of the brain (lacunar state), or the development of a focal infarction. Atherosclerotic changes in the arterial wall reduce the hemodynamic reserve and the adaptation of the vessels of the brain to the changing blood supply conditions, the appearance of a linear dependence of the cerebral circulation on the systemic circulation [21-23]. The urgency of the problem of development and progression of hypertensive cerebral angiopathy in patients is that the development of dysfunction of the system of autoregulation of cerebral blood flow and high blood pressure are underestimated, and even at the initial stages of development of violations contribute to the development of severe complications (Casetta I.A., 2012; Svishchenko Ye.P., 2013; Golovchenko Yu.I., 2014). In patients with hypertensive encephalopathy, the condition of cerebral hemodynamics depends on the state and stability of the mechanisms of regulation of systemic and cerebral hemodynamics, in particular the level of systemic blood pressure, regional cerebral blood flow, the normalization of which in the initial stages of development of disorders prevents the development of severe complications. Waldstein S.R., 2013; Trinus K.F., 2013; Sviridova N.K., 2015), (Parati G.E., 2012 Voloshin P.V., 2015). With prolonged high blood pressure, intracerebral and extracranial arteries are altered, their elastic framework is broken, occurs fragmentation of the intrinsic membrane and destruction of the muscular layer, smooth muscle fibers. As a result, the arteries lengthen, expand, become vorticular, then deform, there are bends and tonsillary stenosis, miliary aneurysms, which creates a real threat of rupture arteries and hemorrhages in the brain.

Prolonged AH leads to a violation penetration of the walls of the vessels, plasmoragiosis, hyalinosis or fibrinoid necrosis. The result of plasmorrhagia and subsequent hemorrhages is sclerosis with gradual narrowing and closure of the lumen of the vessel [32, 34, 35]. Thus, despite the available achievements in diagnosis and treatment chronic cerebral ischemia, there is still no data on structure and dynamics the leading neurological syndromes in patients with AH [1, 2].

Insufficiently studied and features of cerebral blood supply, as well as the relationship of cerebral hemodynamic disorders with structural and morphological changes in the brain. All this necessitates improvement and development of sound diagnostic methods for the development of cognitive impairment **(**CI), to improve the methods of support and increase individual stability of organs and systems of the body, including cerebral hemodynamics under various conditions of its functioning.

Materials and Methods

The study included 60 patients with vascular comorbidity and the presence of addictive cognitive impairment according to the data of the previous psycho-physiological screening. The average age of the subjects was 58,4±2,6 years. The structure of the comorbid pathology was as follows: arterial hypertension - 100%, ischemic heart disease – 71.7% (43 people), dyslipidemia – 85% (51 persons), chronic heart failure – 23,3% (14 people), diabetes – 10% (6 people), overweight and obesity were in 67,3% of the subjects included in the study.

All patients had a comprehensive examination in accordance with the protocols of the Ministry of Health of Ukraine and a neuropsychological examination with an assessment of the CF (MoCA-test) [14, 15, 19, 24, 26, 28]. Hospital scale of anxiety and depression assessment (HADS) was used to exclude depression and to study the level of anxiety. Attention and speed of sensory-motor reactions were investigated by the techniques of "Tables of Schulte" and F.E.Rybakov. Vegetative status was studied according to Wayne's methodology, and the quality of life assessment (QA) was performed by the SF-36 survey. The study of blood flow in the vessels of the head and neck was performed using ultrasound duplex scanning of arteries HDI 7, Philips, USA [9-12, 17, 18, 33, 37]. Patients by simple randomization method (envelope method) were divided into two groups of 30 people. Patients in the 1st st group additionally to personalized antihypertensive therapy received the drugs fenibut 300mg and ipidacrine 5mg (three times a day), patients in the 2nd group personalized antihypertensive therapy only [3-6, 8, 13, 16, 29]. Duration of treatment and observation period - 45 days.

Statistical processing of the results was carried out using the STATISTICA v.6.1® software package (StatsoftInc., USA), with the estimation of the mean values of M, their m errors, the student's criterion, and the reliability of the statistical indicators of the p. Differences were considered to be reliable at $p<0,05$.

Exclusion criteria were:

- necessity of using b-adrenoblockers,
- ischemic and/or hemorrhagic stroke in history,
- a history of cranio-cerebral trauma,
- absorption of alcohol and/or narcotic substances in history,
- cancer disease,
- surgical intervention on the brain in the history,
- presence of contraindications to the use of drugs fenibut or ipidacrine,
- liver disease accompanied by hepatomegaly and/or increased activity of hepatic transaminases and/or increased levels bilirubin,
- recognized anomalies of brachiocephalic vessels, with occlusion lesions of extra-and intracranial arteries,
- hemodynamically significant stenosis trunk
- head and neck arteries,
- difficulty of kidney disease,
- mental illness in history,
- depression.

Results

By age, severity and duration of comorbid vascular pathology and cognitive impairment of the group were comparable.

Characteristic of patients in both groups were the following cardiovascular risk factors: heredity in both groups (69% and 67% respectively) and tobacco smoking (22,8% and 28,6%, respectively) were heavily burdened. In the initial review, the most frequent general complaints in both groups of patients were: sleep disorders (1st group - 27, 2nd group - 23), rapid mood changes (1st group - 19, 2nd group - 25), decrease attention (1st group - 22, 2nd group - 21) and memory (1st group - 24, 2nd group - 8). At the headache in the 1st group, 18 patients were noted, in the 2nd -19, dizziness: in the 1st group - 23 patients, in the 2nd - 26, pain behind the sternum was noted in the 1st group - 15 patients, in the 2nd - 11th, heartbeat – in the 1st group - 17 patients, in the 2nd - 13th.

The average number of points in Wayne in the 1st group was 54, in the 2nd group – 57, after the treatment in the 1st group, the number of points in the Vein questionnaire was 35, which indicates an improvement in the status of vegetative, 2nd group showed a decline in vegetative status, as evidenced by some an increase in points by Wayne (61 points).

In the 1st group, 24 patients had HADS less than 7 points, indicating no anxiety after treatment, 4 patients had from 8 to 10 points, 2 patients – 10-12 points, in contrast to the 2nd group, where there was no anxiety only 3 patients after treatment, 6 patients had 8 to 10 points, 7 patients – 10-12 points, 9 patients 12-15 points, 5 patients had 15 to 18 points, indicating that the high level of anxiety in the 2nd group remained after treatment.

When conducting a study of attention in all patients before the treatment, there were errors in the performance of tasks and in most patients there was an excess of time to perform tasks that is evidence of attention violation. In the 1st group, after the treatment, timing of the tasks has significantly decreased, and the number of errors has become smaller. Namely, the average time for performing the task in Table 1 before treatment was 58,8±4,1 seconds, after treatment the duration decreased to 43,3±3,8 seconds, patients in 1st group were treated for 65,6±4,2 seconds after treatment for 47,9±3,3, Table 3 before treatment – 73,2±6,0, after treatment – 48,1±6,3, Table 4 for 69,0±2.7 seconds was performed before treatment, at 55,8±4,1 after treatment, the table before treatment was 72,2±4.5, after – 51,9±5,2.

In the 2nd group, the time of completion of post-treatment tasks was not statistically different from time-to-time indices, as well as mistakes in the performance of tasks in the study of attention.

Table 3 shows the dynamics of the results of the study of the effectiveness of work, workability and mental stability of patients in 1st group before and after treatment according to the method of "Schultz Tables". After treatment in patients of

1st group, indicators of efficiency, workability and mental stability were significantly higher.

The evaluation of the results of the study of stability and concentration of attention by the method of Rybakov was carried out on the following points:

1. how much time it took for the person tested for the account of the circles in each sector,
2. how well the account itself was right
3. to which sector the account is proved without error.

The degree of concentration of the excitatory process in the visual and motor analyzers, in the account connected with small oculomotor reactions, was investigated.

After treatment in groups 1st and 2nd, there were significant differences in the results of the study by the method of Rybakov. Thus, in the 1st group, up to 5 sectors without errors were performed by 4 patients, in the 2nd group only one patient, up to 4 sectors in the 1st group – 17 patients, 2 – 7, up to 3 sectors in the 1st group – 8, in the 2nd group – 16 patients (the same was before treatment), to 2 sectors without mistakes was counted in the 1st group only 1 patient, and in the 2nd group 2 – 6 patients. This indicates a higher level of stability and concentration in the 1st group.

Table 1: Dynamics of quality of life before and after treatment in the 1st and 2nd groups by questionnaire SF-36 (n = 60)

Indicators, points	1st group		2nd group	
	before treatment	after treatment	before treatment	after treatment
social functioning	49,50±4,88	66,78±6,07	48,90±5,0	50,74±6,97
mental health	60,33±15,11	79,76±10,04	62,76±17,22	67,44±11,27
vitality	59,36±12,82	73,87±11,07	56,40±10,84	61,42±12,77
role- physical functioning	51,23±7,14	84,92±9,34*	50,67±9,12	53,17±16,99
physical functioning	65,16±13,02	88,97±12,09	68,56±17,0	71,87±12,50
pain	54,91±10,41	73,98±9,02	54,14±9,19	63,00±13,58
role-emotional functioning	46,53±10,23	89,28±10,42*	45,98±8,98	47,56±10,56
general health	40,37±10,09	88,44±11,33*	38,75±11,28	49,62±17,40

Note.: * - ($p \leq 0,05$)

When studying quality of life by questionnaire SF-36 (n=60) in study groups, before and after treatment, the following was observed: in the 1st group the level of role physical and role-related emotional functioning and general health significantly increased; in the 2nd group, the standard of living quality did not change significantly.

In the 1st group, quality of life after treatment increased by all indicators, so the social functioning before treatment was 49,5 points, after treatment – 66,8 points, mental health to treatment – 60, 2, after – 79,8 points, the vital force before treatment was 59,3 points, after treatment it became 73,9, the role of physical functioning before treatment – 51,2 points, after treatment – 84, 9 points, physical functioning before treatment – 65, 2, after – 89 points, pain to treatment – 54, 9, pain score after treatment – 74 points, role of emotional functioning before treatment was 46, 5 points, after treatment it was 89, 2 points, general health to treatment – 40,4, after treatment, this figure increased to 88, 4 points.

In the study of the state of cognitive function in patients of the 1st and 2nd groups, cognitive decline was found in all patients. Among the 1st group, the mild CD was registered in 73.3% (22 patients), moderate – in 26.7% (8 patients), among the 2nd group of patients, the mild CD was 76.7%, moderate – in 23.3% of patients.

According to the data of the study of cognitive functions for MoCA in patients of the 1st group, in contrast to patients in the 2nd group there was a significant increase in points in visual-constructive/executive skills (before treatment – 3,94±0,12, after treatment – 4,47±0,11 points), subtotal attention (before treatment – 2,41±0,15, after treatment – 2,97±0,17 points), serial subtraction (before treatment – 1,95±0,15, after treatment – 2, 74±0,13 points), delayed reproduction (before treatment – 3,64±0,16, after treatment – 4,23±0,18 points), orientation (before treatment – 5,57±0,10, after treatment – 5,98±0,11 points) and total score key to treatment – 24,30±0,78, after treatment – 27,65±0,52 points.

According to the ultrasound estimation, it was found that the mean value of intima media complex in patients of the 1 group was 0,98±0,15 cm, in patients of the 2nd group – 0,98±0,12 cm. The rapid measurements in MCA in both groups were statistically comparable. In the course of the ultrasound in patients in the 1st group of patients after the treatment, an increase in the reactivity coefficient was noted at hypercapnic loading (K^+) at 11,34%, with hypokapnic load (K^-) – by 4,07%, the index vasomotor reactivity (IVMR) – by 22,0% ($p \leq 0,05$). In the 2nd group, the growth rate of K^+ was only 6,17%, K^- did not change significantly, and IVMR increased by only 8% ($p > 0,05$).

Conclusions

The drugs of choice for the correction of mild and moderate additive cognitive impairments and improvement of the quality of life in patients with vascular comorbidity are phenibut 300 mg and ipidacrine 5 mg. Drugs should be recommended for course appointment in outpatient practice 3 times a day for up to 45 days 2-3 times a year.

References

1. Akimov GA, Odinak MM. [Differentsialnaya diagnostika nervnyih bolezney]. Moscow. [in Russian], 2000
2. Bugrova SG. [Neyromediatornyie sistemyi i kognitivnyie rasstroystva pri distsirkulyatornoy entsefalopatii]. Fundamentalnyie issledovaniya, 2009; 4:26-28. [in Russian],
3. Burchinskiy SG, Demchenko EV. [Innovatsii v strategii farmakoterapii rannih stadiy kognitivnyih rasstroystv]. Mezhdunarodnyiy nevrologicheskiy zhurnal, 2016; 6(84):137-142. [in Russian].
4. Gromov LO. [FarmakologIchniy profIl dIYi GAMK-ergIchnih preparatIv v ryadu psihotropnih zasobIv]. VIsn. farmakol. Farm, 2001; 11:2-5. [in Russian].
5. Illarioshkin SN. [Vozrastnyie rasstroystva pamyati i vnimaniya: mehanizmyi razvitiya i vozmozhnosti neyrotransmitternoy terapii]?, Nevrologicheskiy zhurnal, 2007; 2:34-40. [in Russian].
6. Kadyikov AS, Shahparonova NV. [Perspektivyi neyroprotektivnoy terpaii v lechenii kognitivnyih narusheniy], CONSILIUM MEDICUM. 2010; 9(12):72-75. [in Russian].
7. Oganov RG. [Komorbidnaya patologiya v klinicheskoy

praktike. Klinicheskie rekomendatsii. Kardiovaskulyarnaya terapiya i profilaktika]. 2017; 16(6):56. [in Russian].
8. Lavretskaya EF. [Neyromidin (amiridin): novyiy tip lekarstvennyih preparatov — stimulyatorov nervnoy i myishechnoy system], Kiyv, 2002, 39. [in Russian].
9. Lelyuk VG, Lelyuk SE. [Vozmozhnosti dupleksnogo skanirovaniya v opredelenii ob'emnyih pokazateley mozgovogo krovotoka], Ultrazvukovaya diagnostika, 1996; 1:24-31. [in Russian].
10. Lelyuk VG, Lelyuk CE. [Tserebrovaskulyarnyiy rezerv pri aterosklerоticheskom porazhenii brahiotsefalnyih arteriy. Etyudyi sovremennoy ultrazvukovoy diagnostiki], Kiev, Ukrmed, 2001 [in Russian].
11. Lelyuk VG, Lelyuk SE. [Tserebralnoe krovoobraschenie i arterialnoe davlenie], Moscow, 2003, 57. [in Russian].
12. Lelyuk VG, Lelyuk CE. [Ehografiya], 2000; 3:271-278. [in Russian].
13. Mehilane LS, Ryago LK, Allikmets LH. [Farmakologiya i klinika fenibuta], T artu, Izd-vo TGU, 1990, 148. [in Russian].
14. Nakaz MOZ. UkraYini vId 19.07.2016 # 736, [Pro zatverdzhennya ta vprovadzhennya mediko-tehnologIchnih dokumentIv zI standartizatsIYi medichnoYi dopomogi pri dementsIYi]. [in Ukrainian].
15. Rubinshneyn SYa. [Eksperimentalnyie metodyi patopsihologii i opit primeneniya ih v klinike. Prakticheskoe rukovodstvo], Moscow, Aprel-Press, 2004. [in Russian].
16. Svintsitskiy AS, Voronkov EG. [Novaya gruppa psihotropnyih sredstv — trankvilizatoryi s nootropnyim komponentom, ih mesto v povsednevnoy vrachebnoy praktike], 2001, 8. [in Russian].
17. Lelyuk VG, Lelyuk CE. [Sostoyanie arterialnoy tserebralnoy gemodinamiki u patsientov s narusheniyami mozgovogo krovoobrascheniya na fone hronicheskoy sistolo-diastolicheskoy arterialnoy gipertenzii] Ehografiya, 2000; 3:271-278. [in Russian].
18. Storozhenko S Yu, Afanasev Yu I. [Otsenka tserebrovaskulyarnoy reaktivnosti u bolnyih arterialnoy gipertenziey], Sovremennyie naukoemkie tehnologii, 2007, 10:40. [in Russian].
19. Khomazyuk TA, Krotova VYu. [Rannya dIagnostika ta korektsIya kognItivnih porushen pri arterIalnIy gIpertenzIYi u patsIentIv pratsezdatnogo vIku]. MaterIali XVII NatsIonalnogo kongresu kardIologIv UkraYini, KiYv, 2016; 3:74. [in Ukrainian].
20. Khomazyuk TA, Krotova V Yu, Soya OV. [ArterIalna gIpertenzIya ta yakIst zhittya: Chi mozhlivo pokraschiti kognItivniy potentsIal patsIEntIv?] MaterIali XVIIINatsIonalnogo kongresu kardIologIv UkraYini, KiYv, 2017, 130. [in Ukrainian].
21. Bogdanova TG, Gippenreyter Yu B, Grigorenko EL. (2002) [Eksperimentalnaya psihologiya: Praktikum: Uchebnoe posobie dlya vuzov], Moscow, Aspekt Press, 2017, 383. [in Russian].
22. Yahno NN, Shtulman DR. [Bolezni nervnoy sistemyi], Moscow, 2005 [in Russian].
23. Aaslid R. Cerebral autoregulation and vasomotor reactivity. Front Neurol. Neurosci. 2006; 21:216-28.
24. Borson S, Scanlan JM, Watanabe J, Tu SP, Lessig MJ. Simplifying detection of cognitive impairment: comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. Am Geriatr Soc, 2005; 53(5):871.
25. Buck D, Jacoby A, Massey A, Ford G. Evaluation of measures used to assess quality of life after stroke. Stroke. 2000; 31:2004-2010.
26. Carotid Evaluation of cerebral AVM s using transcranial Doppler ultrasound. K. F. Lindegaard, S. J. Bakke, P. Grolimund [et al.] J. Neurosurg., 1986; 65:335-344.
27. Cognitive function and overweight in patients with hypertension: are they linked? T.A. Khomazyuk, V. U. Krotova. J Hypertens., 2017; 35(suppl.2):325-326.
28. Diagnosis and treatment of cognitive disorders in arterial hypertension. T.A. Khomazyuk, V. U. Krotova. J Hypertens, 2016; 34(Suppl. 1):234.
29. Ellergast JP. Gamma-aminobutyric acid — mediated neurophysiological effects in the central nervous system. Brain neurophysiology. Chicago: Illinois Univ. Press, 2000, 497-530.
30. Fayers PM, Machin D. Quality of life: Assessment, analysis, and interpretation. John Wiley & sons, England, 2000.
31. Fayers PM, Sprangers MA. Understanding self-rated health. Lancet. 2002, 359:187-188.
32. Frost L, Andersen LV, Johnsen SP, Mortensen LS. Lost life years attributable to stroke among patients with nonvalvular atrial fibrillation: a nation-wide population-based follow-upstudy. Neuroepidemiology. 2007; 29:59-65.
33. Giller CA. A bedside test for cerebral autoregulation using transcranial Doppler ultrasound, Acta Neurochir, 1991; 108(1-2):7-14.
34. Larrieu S, Letenneur L, Orgogozo JM. Incidence and outcome of mild cognitive impairment in a population-based prospective cohort. Neurology 2002; 59:1594-99.
35. Medically reviewed by TimothyJ. Legg, PhD, PMHNP-BC on March 11, Writtenby Erica Cirino, 2016.
36. Nilsson PM. Early vascular agingin translation: from laboratory investigations to clinical applications in cardiovascular prevention. J Hypertens. 2013, 31(8):1517-1526.
37. Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM et al; Health ABC Study. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation. 2005; 111:3384-3390.
38. Syndrome cognitive impairment and quality of life in patients with hypertension. T.A. Khomazyuk, V. U. Krotova, O.V. Soya, T.V. Lakiza. J Hypertens. 2016; 34(Suppl. 2):227.