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Impact of Citicoline over Cognitive Impairments after General Anesthesia

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Abstract: ***Postoperative cognitive delirium - POCD is chronic damage with deterioration of the memory, the attention and the speed of the processing of the information after anesthesia and operation. It is admitted that anesthetics and other perioperative factors are able to cause cognitive impairments through induction of apoptosis, neuro-inflammation, mitochondrial dysfunction and so on. More and more medicaments are used in modern medicine, as, for instance, Citicoline, which are in a position significantly to reduce this unpleasant complication of the anesthesia.***

Keywords: Postoperative cognitive delirium, anesthesia, Citicoline.

1. Introduction

It is known that anesthetics and other perioperative factors are able to cause cognitive impairments through induction of apoptosis, neuro-inflammation, mitochondrial dysfunction and so on.
Chronic damage with deterioration of the memory, the attention and the speed of the processing of the information after anesthesia and operation is understood under the title Postoperative cognitive delirium - POCD. (1)
Monk and colleagues report on the availability of POCD in patients discharged from hospital in the following ratio:

- 36, 6 % of surgical patients aged 18-39 years;
- 30, 4 % of the patients aged 40-59 years;
- 41, 4 % of the people aged 60 and over. (2)

The conclusion that age is the main risk factor for the development of POCD may be drawn from here. (3)

The mechanisms resulting in cognitive damage after anesthesia and operative interference are still unclarified. The impact of the immune system (TNF-α) NF-yB in the signal cascade with the release of cytokines which impair the blood-brain barrier and the role of the inflammatory response which developed directly after the anesthesia and the operative interference are admitted. (4), (5)

Medicament Citocoline has been more and more frequently successfully applied in the last few years aimed at the reduction of the frequency of POCD.

It is a medicament which renders its effect through exerting impact over the phospholipids of the neural membranes, through which the transfer of the nervous impulse and the neuro-transmission is realized. (6), (7), (8), (9), (10), (11), (12)

Therefore, Citocoline is the main intracellular precursor of phospholipid phosphatidyl choline. (13), (14), (15), (16), (17), (18), (19), (20), (21), (22), (23), (24), (25), (26)

It exerts impact over the cholinergic system and acts as a choline donor for the enhanced synthesis of acetylcholine.

2. Materials and Methods

46 patients with various diagnoses were investigated, operated through a laparoscopic surgical method during the period 2019 in the University Multi-Profile Active Treatment Hospital Sveta (Saint) Marina – town of Pleven aged between 33 years and 83 years.

General anesthesia was performed on all the patients in conformity with the protocol: pre-medication with Midazolam and Fentanyl, input with Propofol, Succinylcholine and maintenance of the anesthesia with Atracurium, Fentanyl and Sevoflurane in the usual dosages.

The patients were divided into two groups:
First group - 24 patients whom Citicoline was applied to 30 minutes prior to the end of the anesthesia and on the first and second postoperative days.
Second group - 22 patients whom Citicoline was not applied to.

The availability of an impaired cognitive function was investigated during the postoperative period on the first and second postoperative days, and simple mathematical equations were given to the patients for solution.

The frequency distribution of the patients per diagnoses is presented in Fig. 1 and Fig. 2.

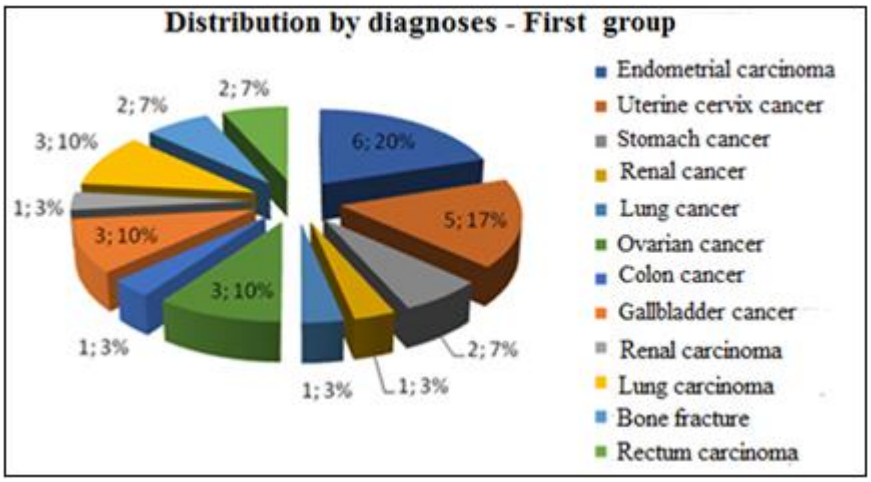

Figure 1: Frequency distribution of the patients from the first group in conformity with diagnoses

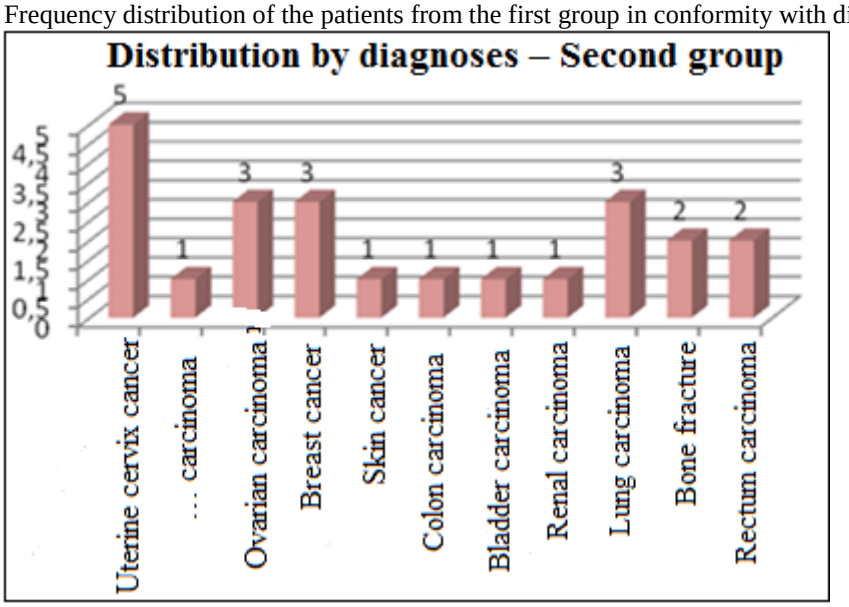

Figure 2: Frequency distribution of the patients from the second group in conformity with diagnoses

The patients in the two investigated groups per gender are presente in Fig. 3.

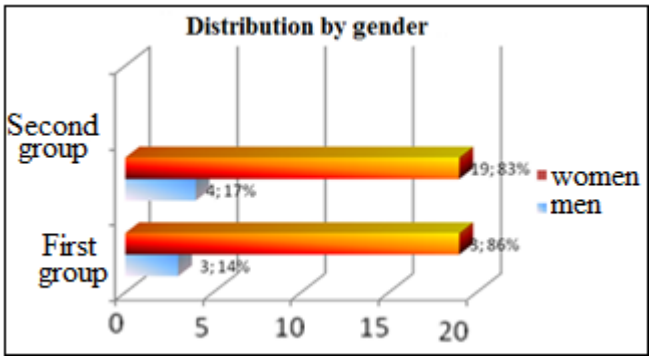

Figure 3: Distribution of the patients in the two groups in conformity with their gender

3. Results

Alopsychic and autopsychic disorientation, amnesia and impossibility to solve the problems assigned appeared in the first group in two patients (aged 68 years and 79 years) (Fig. 4).

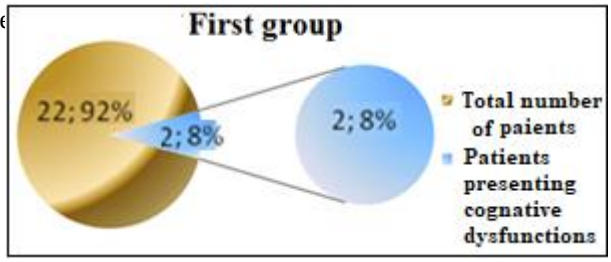

Figure 4: Patients from the first investigated group who developed cognitive deficit after application of Citicoline

In the second group PODC was registered in 5 patients (aged 71, 83, 70, 71 and 63 years) (Fig. 5).

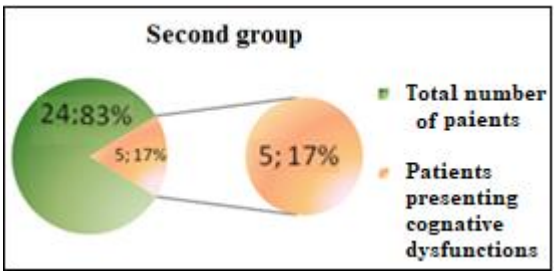

Figure 5: Percentage distribution of the patients from the second investigated group who developed cognitive impairments after general anesthesia

4. Discussion

A number of clinical studies on the impact of Citicoline over the cognitive impairments were conducted. (27), (28)

Most authors announce that Citicoline is exceptionally well tolerated by the patients. (29), (30). Hurtado O. and colleagues prove that the continuous treatment with Citicoline improves the functional recovery after experimentally caused insult and it manages significantly to increase the plasticity of the neurons which results in clinical improvement of the patients with a stroke. (31)

5. Conclusion

POCD is an unfavorable complication of the anesthesia which is frequently associated with the old age of the patients, the accompanying diseases as the cerebrovascular disease, experienced in the past stroke, big in volume surgical operations and so on. A number of studies conducted in the last few years have proven that POCD is the reason for impaired quality of life, disability and high percentage of lethality after the operative interference.

The application of various medicaments, which reduce the risk of postoperative development of POCD, is more and more preferred in ICU.

Great hope in this respect is placed on medicament Citicoline which turned out to have big advantages as compared to the remaining medicaments, which with regard to their effect are inferior to it.

References

[1] Vutskits L, Xie Z. Lasting impact of general anaesthesia on the brain: mechanisms and relevance . Nat Rev Neurosci.2016;17(11):705-717.
[2] Monk TG, Saini V, Weldon BC, Sigl JC. Anesthetic management and one-year mortality after noncardiac surgery. Anesth Analg. 2005;100:4–10.
[3] Ingrid Rundshagen. Postoperative Cognitive Dysfunction. Dtsch Arztebl Int . 2014 Feb; 111(8): 119–125.
[4] 4.Moller JT, Cluitmans P, Rasmussen LS, et al.Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study.Lancet.1998;25:857–861.
[5] Seitz DP., Shah PS., Hermann N., Sdidiqui N. Exposure to general anesthesia and risk of Alzheimer's disease: a systematic review and meta-analysis. BMC Geriatr. 2011 Dec 14;11:83. doi: 10.1186/1471-2318-11-83.
[6] Cramer SC, Finkelstein SP. 1999. Reparative approaches: growth factors and other pharmacological treatments. In: Miller LP (ed) Stroke therapy: basic, preclinical, and clinical directions. Wiley-Liss, NY, USA, pp 321-336. 68.
[7] Zweifler RM. 2002. Membrane stabilizer: citicoline. Curr Med Res Opin 18(Suppl 2): S14-S17. https://doi.org/10.1185/030079902125000679
[8] McDaniel MA, Maier SF, Einstein GO. 2003 . 'Brain-specific' nutrients: a memory cure? Nutrition 19(11-12): 957-975. https://doi. org/10.1016/S0899-9007(03)00024-8 9. Mamoun CB, Prigge ST, Vial H. 2010. Targeting the lipid metabolic pathways for the treatment of malaria. Drug Dev Res 71(1): 44-55. https://doi.org/10.1002/ddr.20347
[9] 10. Candelario-Jalil E. 2009. Injury and repair mechanisms in ischemic stroke: considerations for the development of novel neurotherapeutics. Curr Opin Investig Drugs 10(7): 644-654.
[10] 11. Saver JL. 2010. Targeting the brain: neuroprotection and neurorestoration in ischemic stroke. Pharmacotherapy 30: S62-S69. http://doi.org/10.1592/phco.30.pt2.62S.
[11] 12. Julio J Secades. Citicoline in the Treatment of Cognitive Impairment. Journal of Neurology & Experimental Neuroscience. Article. January 2019. P. 14-26.
[12] 13. Grieb P. 2014. Neuroprotective properties of citicoline: facts, doubts and unresolved issues. CNS Drugs 28(3): 185-193. https://doi.org/10.1007/ s40263-014-0144-8 74. De la Morena E, Goldberg DM, Werner M. 1985. Citidindifosfato de colina y biosíntesis de fosfolípidos. In: De la Morena E (ed) Citicolina: bioquímica, neurofarmacología y clínica. Salvat, Barcelona, Spain, pp 25-38.
[13] 14. Chida N, Shimizu Y. 1973. Biosynthesis of myelin lipids of cultured nervous tissues. Incorporation of choline and CDPcholine into myelin phospholipids. Tohoku J Exp Med 111(1): 41-49. https://doi. org/10.1620/tjem.111.41
[14] 15. Marggraf WD, Anderer FA. 1974. Alternative pathways in the biosynthesis of sphingomyelin and the role of phosphatidylcholine, CDPcholine and phosphorylcholine as precursors. HoppeSeyler's Z Physiol Chem 355(7): 803-810. https://doi.org/10.1515/ bchm2.1974.355.2.803
[15] 16. Vance DE, Pelech SL. 1985. Cellular translocation of CTP: phosphocholine cytidylyltransferase regulates the synthesis of CDPcholine. In: Zappia V, Kennedy EP, Nilsson BI, Galletti P (eds) Novel biochemical, pharmacological and clinical aspects of cytidinediphosphocholine. Elsevier Science Publishing, Amsterdam, Netherlands, pp 15-24.
[16] 17. Goracci G, Francescangeli E, Mozzi R, Porcellati S, Porcellati G. 1985. Regulation of phospholipid metabolism by nucleotides in brain and transport of CDPcholine into brain. In: Zappia V, Kennedy EP, Nilsson BI, Galletti P (eds) Novel biochemical, pharmacological and clinical aspects of cytidinediphosphocholine. Elsevier Science Publishing, Amsterdam, Netherlands, pp 105-116.
[17] 18. George TP, Cook HW, Byers DM, Palmer FBSC, Spence MW. 1991. Channeling of intermediates in CDP-choline pathway of phosphatidylcholine biosynthesis in cultured glioma cells is dependent on intracellular Ca2+. J Biol Chem 266: 12419-12423.
[18] 19. Murphy EJ, Horrocks LA. 1993. CDPcholine, CDPethanolamine, lipid metabolism and disorders of the Central Nervous System. In: Massarelli R, Horrocks LA, Kanfer JN, Löffelholz K (eds) Phospholipids and signal transmission. Springer-Verlag, Berlin, Germany, pp 353-372.
[19] 20. Tronchère H, Record M, Tercé F, Chap H. 1994. Phosphatidylcholine cycle and regulation of

phosphatidylcholine biosynthesis by enzyme translocation. Biochim Biophys Acta 1212(2): 137-151. https://doi. org/10.1016/0005-2760(94)90248-8

[20] 21. Weiss GB. 1995. Metabolism and actions of CDP-choline as an endogenous compound and administered exogenously as citicoline. Life Sci 56: 637-660.

[21] 22. Jackowski S, Wang J, Baburina I. 2000. Activity of the phosphatidylcholine biosynthetic pathway modulates the distribution of fatty acids into glycerolipids in proliferating cells. Biochim Biophys Acta 1483(3): 301315. https://doi.org/10.1016/S1388-1981(99)00203-6.

[22] 23. Dowd SR, Bier ME, Patton-Vogt JL. 2001. Turnover of phosphatidylcholine in Saccharomyces cerevisae. The role of the CDPcholine pathway. J Biol Chem 276: 3756-3763. https://doi.org/10.1074/ jbc.M003694200.

[23] 24. Henneberry AL, Wright MM, McMaster CR. 2002. The major sites of cellular phospholipid synthesis and molecular determinants of fatty acid and lipid head group specificity. Mol Biol Cell 13(9): 3148-3161. https:// doi.org/10.1091/mbc.01-11-0540. 25. Hunt AN, Clark GT, Neale JR, Postle AD. 2002. A comparison of the molecular specificities of whole cell and endonuclear phosphatidylcholine synthesis. FEBS Lett 530: 89-93. https://doi. org/10.1016/S0014-5793(02)03429-4.

[24] 26. Gibellini F, Smith TK. 2010. The Kennedy pathway –de novo synthesis of phosphatidylethanolamine and phosphatidylcholine. IUBMB Life 62(6): 414-428.

[25] 27. García-Cobos R, Frank-García A, Gutiérrez-Fernández M, DíezTejedor E. 2010. Citicoline, use in cognitive decline: vascular and degenerative. J Neurol Sci 299(1-2): 188-92.

[26] 28. Gareri P, Castagna A. 2017. Citicoline in vascular cognitive impairment: some latest evidences. Ann Alzheimers Dement Care 2(1): 018-019.

[27] 29. Fioravanti M, Yanagi M. Cytidinediphosphocholine (CDP-choline) for cognitive and behavioural disturbances associated with chronic cerebral disorders in the elderly. Cochrane Database Syst Rev2005; *18*:CD000269.

[28] 30. Fioravanti M, Buckley AE. Citicoline (Cognizin) in the treatment of cognitive impairment. Clin Interv Aging**.**2006; *1*:247–251.

[29] 31. Hurtado O, Cárdenas A, Pradillo JM, Morales JR, Ortego F, Sobrino T, Castillo J, Moro MA, Lizasoain I. A chronic treatment with CDP-choline improves functional recovery and increases neuronal plasticity after experimental stroke. **Neurobiol Dis**. 2007; *26*:105–111.