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Therapeutic Correlation, Choline Derivatives GABA, Break Through Treatment of Stroke

Ishaq Khan*, Junaid Khan, Sameera I Khan, Imran Khan Munir, Shah Fahad Khan, Rohail Khan

Mediks International Hospital, Islamabad, Pakistan.

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ABSTRACT

In the past few decades, modern advancements made in medical field have given rise to treatment protocols ensuring maximum recovery and minimum mortality rate. Stroke or cerebrovascular accident is a clinical condition manifested as paralysis of either half or full human body, loss of voluntary movements, spastic and hypertonic muscles along with slurred speech, dysphagia and sometimes prolonged periods of unconsciousness as well. Previously it was thought that stroke is not curable and there is only supportive medication available for it capable of preventing further worsening as there was no clinical medicine or agent available that could reverse the pathology. In last ten years USA, Japan and Europe enhanced the clinical usage of Cytidine-5'-diphosphocholine (CDP-choline) prompt and complete treatment of stroke patients. These choline molecules are readily available in two basic forms i.e., free CDP choline or Liposome encapsulated choline molecules having increased intake rate by damaged brain tissue for preventing further break down of brain phospholipids and reduces cerebral edema. As per results of our clinical survey patients who were administered with free CDP choline molecules showed less recovery as compared to those who were administered with liposome encapsulated choline molecules as these molecules had more enhanced capacity to reduce cerebral ischemia and brain swelling.

Keywords: Free CDP-Choline, Phospholipid breakdown, Cerebral edema, Cerebral ischemia, Liposome covered choline molecule

Abbreviations: CT: Computerized Tomography; MRI: Magnetic resonance imaging; TIA: Transient Ischemic Attack; SPSS: Statistical Package for the Social Sciences

INTRODUCTION

Choline and its derivatives have been known as significant medication which is monetarily accessible as curative treatment protocol in Western countries since last two decades. Choline molecules have demonstrated useful impacts in cerebral ischemia [1] along with enhanced recovery ratio in cases of spastic paralysis i.e. hemiplegic, diaplegic and paraplegic cases [2]. Clinical preliminaries in Spain and Italy demonstrated that choline uptake by damaged brain tissues resulted in improved recuperation; while researches conducted in regions of Germany and USA [3] have given questionable outcomes. Western world has been indulged in conducting clinical experiments on therapeutic effects of choline knowing it's an impressively curative medicine for stroke, since stroke is the 4th principal reason of death in entire western world. It indorses disability and handicapped population in a nation adding socioeconomic burden [4]. Choline derivatives have emerged as a magical invention owing to their ability of reducing cerebral ischemia and edema by decreasing phospholipid breakdown ratio [5]. Hydrolysis of CDP-choline results in formation of cytidine and choline easily taken by brain tissues as they cross blood-brain barrier [6]. Previous researches concluded that administration of either exogenous choline molecules or liposome covered molecules within one hour of Transient Ischemic Attack (TIA) as more the time passes, cerebral ischemia expands

Corresponding author: Ishaq Khan, Mediks International Hospital, Islamabad, Pakistan, Tel: 202-873-3397; E-mail: ishaqkhan1@gmail.com

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and involves more of the brain tissue [7]. Previous studies suggest that the efficacy of liposome encapsulated choline molecules in reducing size of cerebral infarct if administered within 24 h of TIA or ischemic stroke attack is much more as compared to free choline molecules. In current study patients who received infusion of liposome covered choline molecules manifested better and prompt recovery. A clinical survey trial reported that patients receiving choline molecules as their foremost treatment of stroke had fast rate of recovery as administration of CDP-choline reduces process of phospholipid break down and promotes phospholipid synthesis [8]. In USA multiple researches have been conducted to evaluated beneficial properties of choline derivative (citicoline) in treatment of cerebral ischemia and how it reduces size of cerebral infarct and rate of phospholipid breakdown. Previous researches suggest that mortality rate in stroke patients treated with citicoline is greatly reduced [9]. The sole motivation behind this investigation is to create mindfulness with respect to helpful treatment of CDP choline in hypertensive patients and its effect in diminishing stroke episode in hypertensive guys and females. There isn't any such investigation directed beforehand in Pakistan featuring the helpful utilization of choline subordinates [10-15].

MATERIALS & METHODS

Study subjects

We conducted a clinical survey from October 2017 to October 2018. Cases, 162 stroke patients, i.e., both males and females were chosen from the patients admitted to Mediks international Hospital, Islamabad, Pakistan. All cases were first-ever stroke patients and were diagnosed on the basis of computerized tomography (CT)-scan and Magnetic resonance imaging (MRI) reports [16-23].

Patients who were treated with either free CDP molecules or liposome encapsulated choline molecules fulfilling inclusion criterion (aged between 45-75, diabetic, hypertensive, post-menopausal and osteoporotic) were enrolled in the study via simple convenient sampling after signing informed consent [24-26].

Statistical analysis

A specially designed questionnaire having two parts was used, 1st part containing demographic details, history of associated co-morbidities and risk factors was filled for all the patients. Second part of the questionnaire was regarding variant treatment protocols patients have been through and what prospective outcomes they had. Two specific treatment methods were taken into consideration, i.e., administration of 500 mg/kg of CDP-choline in 5 ml of 0.9% saline, intraperitoneally, 24 hourly and 1 hourly prior to middle cerebral artery occlusion [27]. Second treatment protocol observed was Liposome typified CDP-choline administration after 1 h transient center cerebral vein impediment and 24-hourly reperfusion in unexpectedly hypertensive patients. Immunohistochemistry reports of all the patients were observed for drawing results regarding efficacy of both treatment protocols. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23. Descriptive Statistical data was analyzed by SPSS version 23. In data analysis, mean ¬+ standard deviation was calculated for quantitative variables and frequency/percentages were calculated for categorical variables.

RESULTS

The aim of this study was to evaluate the therapeutic correlation of choline derivatives in treatment of stroke. **Figure 1** and **Table 1** shows age and gender characteristics of stroke patients enrolled in the study with an overall predominance of female gender, i.e., 105, 64.8% and males were 57, 35.1% out of total 162 patients, the age range was from 45-75 with mean age of 60.

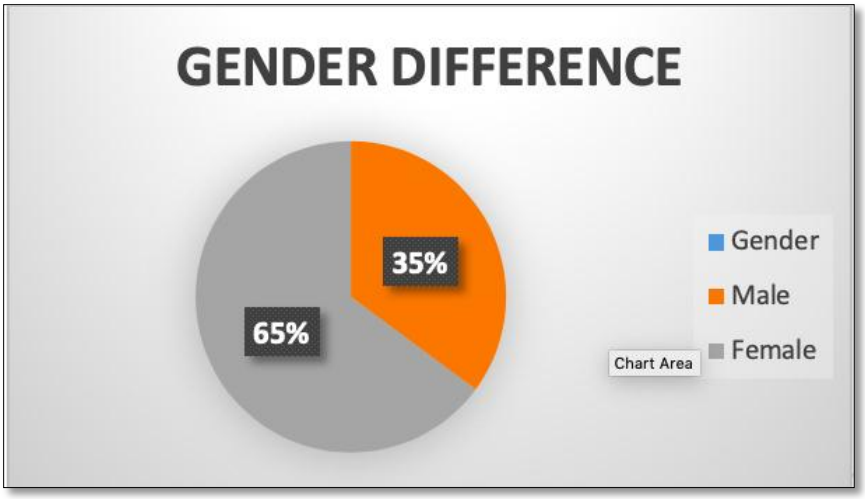

Figure 1. shows percentage of male and female stroke patients.

Table 1. Demographic characteristics of patients.

Gender	**Frequency**	**Percentage**
Male	57	35.1%
Female	105	64.8%
Age Characteristic		
Age range	45-75	
Mean age	65.26±5.40	

Table 2 shows that l administration of CDP choline within 24 h after ischemic stroke results in reduction of phosphorylation.

Table 2. Frequency table showing reduction in phosphorylation from administration of CDP-choline and 0.5 ml saline solution in study subjects.

Variables	**Frequency of reduction of phosphorylation in N=162**	**p-value**
500mg/kg CDP-Choline in 0.5ml of 0.9% saline solution	145, 89%	0.001
0.5 ml of 0.9% saline solution	17, 10%	0.0742

Table 3 shows that liposome encapsulated choline reduces size of infarction with more efficacy as compared to free choline molecules. A p-value of less than 0.01 shows that results are highly significant.

Table 3. Liposome encapsulated choline versus free choline derivatives in reducing size of infarction.

Variables	**Frequency of reduction of size of infarction in N=162**	**p-value**
Liposome encapsulated choline	62%	0.001
Free choline derivatives	26%	0.001

DISCUSSION

The sole purpose of conducting this research was to develop awareness regarding miraculous effects of choline to cure ischemic stroke and enhance process of recovery. Variant researches on beneficial effects of choline and its sub-ordinates have been conducted all over the world but unfortunately very little or no work has been done on it in Pakistan. We conducted this clinical survey to promote awareness regarding its benefits and to help people who have given up on their lives thinking stroke is not curable. Our research results cannot be generalized to entire population of Pakistan as people living in peripheral areas cannot be benefited by this advanced treatment protocol and tertiary medical centers are still following old standard treatment methods depriving people of basic health facilities. It is our moral obligation to spread awareness regarding advanced treatment methods making people sure that stroke is curable. The stereotype treatment protocols must be abolished and physicians should adapt modern treatment methods as being followed all over the world for betterment of their people. We all need to get together on a single platform to ensure advanced medical care facilities to people who are underprivileged and underserved in terms of basic facilities and necessities.

CONCLUSION

Choline molecules serve an important role in reduction of size of infarction and early recovery in stroke patients provided that it is administered within 24 h after attack of stroke.

REFERENCES

1. Weiss SB, Smith SW, Kennedy EP (1958) The enzymatic formation of lecithin from cytidine diphosphate choline and D-1, 2-diglyceride. J Biol Chem 231: 53-64.

2. Gibellini F, Smith TK (2010) The Kennedy pathway-de novo synthesis of phosphatidylethanolamine and phosphatidylcholine. IUBMB Life 62: 414-428.

3. Hunt AN, Clark GT, Attard GS, Postle AD (2001) Highly saturated endonuclear phosphatidylcholine is synthesized in situ and colocated with CDP-choline pathway enzymes. J Biol Chem 276: 8492-8499.

4. Kent C, Carman GM (1999) Interactions among pathways for phosphatidylcholine metabolism, CTP synthesis and secretion through the Golgi apparatus. Trends Biochem Sci 24: 146-150.

5. Berger L, Gimenez WT (1956) Crystallization of cytidine diphosphate choline from yeast. Science 124: 81.

6. Ansell GB, Bayliss BJ (1961) The cytidine diphosphate choline content of rat brain. Biochem J 78: 209-213.

7. Manaka S, Sano K, Fuchinoue T, Sekino H (1974) Mechanism of action CDP-choline in parkinsonism. Experientia 30:179-180.

8. Horrocks LA, Dorman RV, Dabrowiecki Z, Goracci G, Porcellati G (1981) CDP choline and CDP ethanolamine prevent the release of free fatty acids during brain ischemia. Prog Lipid Res 20: 531-534.

9. Horrocks LA, Dorman RV, Dabrowiecki ZM (1981) Therapeutic agents for preventing phospholipid degradation and free fatty acid proliferation. United States Patent No: 4,386,078.

10. García-Cobos R, Frank-García A, Gutiérrez-Fernández M, Díez-Tejedor E (2010) Citicoline, use in cognitive decline: Vascular and degenerative. J Neurol Sci 299: 188-192.

11. Alvarez-Sabín J, Román GC (2011) Citicoline in vascular cognitive impairment and vascular dementia after stroke. Stroke 42: S40-S43.

12. Arenth PM, Russell KC, Ricker JH, Zafonte RD (2011) CDP-choline as a biological supplement during neurorecovery: A focused review. PMR 6: S123-S131.

13. Hurtado O, Lizasoain I, Moro MÁ (2011) Neuroprotection and recovery: Recent data at the bench on citicoline. Stroke 42: S33-S35.

14. Secades JJ (2012) Probably role of citicoline in stroke rehabilitation: Review of the literature. Rev Neurol 54: 173-179.

15. Schauss AG, Somfai-Relle S, Financsek I, Glavits R, Parent SC, et al. (2009) Single- and repeated-dose oral toxicity studies of citicoline free-base (choline cytidine 5'-pyrophosphate) in Sprague-Dawley rats. Int J Toxicol 28: 479-487.

16. Cho HJ, Kim YJ (2009) Efficacy and safety of oral citicoline in acute ischemic stroke: Drug surveillance study in 4,191 cases. Methods Find Exp Clin Pharmacol 31: 171-176.

17. Dávalos A, Castillo J, Alvarez-Sabín J, Secades JJ, Mercadal J, et al. (2002) Oral citicoline in acute ischemic stroke: An individual patient data pooling analysis of clinical trials. Stroke 33: 2850-2857.

18. Galletti P, De Rosa M, Cotticelli MG, Morana A, Vaccaro R, et al. (1991) Biochemical rationale for the use of CDP choline in traumatic brain injury: Pharmacokinetics of the orally administered drug. J Neurol Sci 103: S19-S25.

19. Galletti P, De Rosa M, Nappi MA, Pontoni G, del Piano L, et al. (1985) Transport and metabolism of double-labelled CDPcholine in mammalian tissues. Biochem Pharmacol 34: 4121-4130.

20. López-Coviella I, Agut J, Savci V, Ortiz JA, Wurtman RJ (1995) Evidence that 5′-cytidinediphospho-choline can affect brain phospholipid composition by increasing choline and cytidine plasma levels. J Neurochem 65: 889-894.

21. Sarkar AK, Ghosh D, Haldar D, Sarkar P, Gupta B, et al. (2012) A rapid LC-ESI-MS/MS method for the quantitation of choline, an active metabolite of citicoline: Application to in vivo pharmacokinetic and bioequivalence study in Indian healthy male volunteers. J Pharm Biomed Anal 71: 144-147.

22. Bligh J (1951) The level of free choline in plasma. J Physiol 117: 234-240.

23. Adamczyk M, Brashear RJ, Mattingly PG (2006) Choline concentration in normal blood donor and cardiac troponin-positive plasma samples. Clin Chem 52: 2123-2124.

24. Glunde K, Serkova NJ (2006) Therapeutic targets and biomarkers identified in cancer choline phospholipid metabolism. Pharmacogenomics 7: 1109-1123.

25. EFSA (2011) Panel on Additives and Products or Substances used in Animal Feed (FEEDAP). Scientific opinion on safety and efficacy of choline chloride as a feed additive for all animal species. EFSA J 9: 2353.

26. Food Safety Authority of Ireland (2012) Safety assessment of citicoline.

27. Johansson M, Van Guelpen B, Vollset SE, Hultdin J, Bergh A (2009) One-carbon metabolism and prostate cancer risk: Prospective investigation of seven circulating B vitamins and metabolites. Cancer Epidemiol Biomark Prev 18: 1538-1543.