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Alcohol Impedes Neuroplasticity and Functional Recovery after Stroke

Poonam Chaturvedi*

Department of Neurology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

***Corresponding author:** Poonam Chaturvedi

drrmlims.pfms@gmail.com; poonamchaturvediphysio@gmail.com

Department of Neurology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

Tel: +9451149311

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Abstract

Background: Recovery after stroke depends upon neurogenesis, angiogenesis and synaptogenesis known as neuroplasticity. Neurotrophins play very important role in neuroplasticity but it can be affected by several risk factors such as diabetes mellitus (DM), hypertension, smoking and alcohol consumption. In this study we tried to find out the most significant risk factor which severely affect stroke outcome and neuroplasticity.

Subjects and methods: In this study 208 patients with stroke were recruited and divided into two groups according to presence and absence of risk factors such as diabetic- non diabetic; hypertensive- non hypertensive; with and without both DM+ hypertension and alcoholic- non =alcoholic. We used Functional Independence Measure (FIM) Scale to assess functional recovery and Serum Brain Derived Neurotrophic Factor (S. BDNF) to assess neuroplasticity in each patient.

Results: Alcohol is the most significant risk factor which affect the stroke outcome severely. Non- alcoholic patients showed better recovery and higher serum BDNF levels than alcoholic patients. The improvement was highly significant both after two weeks (p=.025) and at six months (p=.001). Lower serum levels of BDNF were observed in group 1 at admission (Group. 1=8.51 ± 4.26 ng/ml; group 2=(10.34 ± 3.96 ng/ml, p=.001). FIM score in alcoholics 34.66 ± 9.81 to 60.33 ± 15.31 and in non- alcoholics 39.48 ± 19.30 to 68.24 ± 20.29, p=.03). Alcohol was found a significant risk factor for poor outcome (F (2.5), p=.023).

Conclusion: These findings suggest us that alcohol slows down the process of neuroplasticity and is a risk factor for poor outcome after stroke.

Keywords: Stroke; Alcohol; Neuroplasticity; Outcome

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Introduction

Alcohol consumption is one of the major forms of addiction. According to WHO reports of 2014, alcoholism alone causes 5.9% deaths every year and the burden of the disease accounting to 5.1% [1]. Drinking alcohol is associated with the risk of developing health problems such as liver cirrhosis, cardiovascular diseases and cancer [2-5]. The over consumption of alcohol can also have serious social and economic consequences for the individual, family as well as for the society [6]. Heavy drinkers are those consuming 5 or more drinks on the same occasion on each of 5 or more days in the past 3 years. Liver plays an important role in lipid metabolism. Marked alterations in lipid metabolism have been reported on chronic alcoholics [7]. Altered lipid metabolism is the risk factor for atherogenesis. Excess risk of incident atherosclerosis observed among heavy alcohol consumers (> or =100 g/d) [8].

Alcohol consumption also affects musculoskeletal system. The acute and chronic effects of alcohol on bone, muscle and peripheral nerves include traumatic fractures, osteoporosis and osteonecrosis. In muscle, a sustained bout of heavy drinking may cause rhabdomyolysis, while chronic alcohol use may produce proximal myopathy. In peripheral nerves, acute alcohol intoxication may lead to pressure neuropathy and chronic abuse may cause peripheral neuropathy [9]. Development and survival of neurons in the central nervous system are regulated by many extracellular factors. Neurotrophins play a significant role in the proliferation,

migration, and differentiation of cells (neurogenesis) and ensure their functional and structural integrity. Neurotrophins include Brain-Derived Neurotrophic Factor (BDNF), nerve growth factor (NGF), neurotrophin-3 (NT-3), and neurotrophin 4/5 (NT4/5) [10, 11] BDNF is a factor determining the model of neurological damage and the possibility of neurological improvement after mechanical injury and ischemic damage. BDNF concentration correlates with the degree of vasogenic damage to white matter of the brain. According to recent studies, genotype plays a role in the prognosis of improved mobility after stroke [12].

The results of previous studies about impact of alcohol consumption on functional outcome and serum level of BDNF are both supportive and conflicting. So the present study aims to evaluate the effects of alcohol consumption on functional recovery and neuroplasticity (S. BDNF) in patients with stroke [13].

Materials and Methods

A total of 245 patients with first ever stroke were included in this prospective study. Patients were recruited from department of neurology in our hospital. The study was approved by the ethical committee of the institution. Out of 245, only 208 patients were available at the end of six months for analysis. Patients were divided into two groups group 1 (alcoholic n=48) and group 2 (non-alcoholic n=160) on the basis of history of alcohol consumption. An approved written informed consent was signed by all subjects prior to inclusion into study.

All study subjects underwent analysis in terms of the following:

Demographic assessment

a) Patient's age, gender, side affected and type of stroke at the time of admission.

b) Neurological status at the time of admission according to NIHSS (National Institutes of Health Stroke Scale) in ischemic stroke and Intracerebral Hemorrhage score (ICH) in hemorrhagic stroke;

Clinical assessment

a) Assessment of Functional Independence Measure Scale Scores (FIM) and modified Rankin Scale Scores (mRS) at admission.

b) Assessment of triglycerides, cholesterol, HDL, LDL and VLDL.

Assessment of serum BDNF level

2.0 ml of blood sample was taken from each patient and allowed to stand for one hour. Serum was separated by centrifugation of whole blood at 1500 g and stored at −80°C until further processing. Serum BDNF level was quantified by using commercially available ELISA kit (Ray Biomed Human BDNF ELISA kit). This ELISA kit is based on standard sandwich enzyme- linked immunosorbent assay technology. Seven standard concentrations (2000, 1000, 500, 125, 62.5, 31.2 and 0 ng/ml) were assessed for corresponding OD values and a standard curve was generated. OD values of samples were read by the ELISA reader at wavelength 450 nm.

The value of BDNF comes out in pictogram/milliliter (pg/ml) which was then converted into nanogram/milliliter (ng/ml).

Statistical analysis

We used Statistical Package for the Social Sciences (SPSS) 20.0 to analyze the data. Charts were plotted by Graphpad PRISM. The values in our data were normally distributed, so we applied parametric tests to analyze the data. Descriptive statistics was used to calculate mean and standard deviations. We used independent t- test to compare means in between two groups. Chi- square test was used to compare the nominal data in between groups. Multiple regressions were used to assess risk factors for poor outcome after stroke. A p value of <0.05 was taken significant to draw our conclusion.

Results

Mean age of the subjects in group 1 was 56.29 ± 11.06 (Range 30-75 years) and in group 2 was 57.42 (10.35) years **(Table 1).** In group 1 all subjects were males and in group 2, 40 females and 120 males were there. The reason for only male patient in alcoholic group is that in Uttar Pradesh there is no culture of drinking alcohol amongst. We did not find any female with drinking history in our study. In both groups most of the patients had middle cerebral artery (MCA) stroke. The number of hypertensive and diabetics were more in alcoholic group. Dyslipidemia was found more in alcoholics. Mean NIHSS score was 9.46 ± 5.17 (Range 1- 25). All subjects were oriented to time place and person, GCS 14.75 ± 0.21. Mean Serum BDNF level at the time of admission was 9.93 ± 4.04 ng/ml. FIM scores were not significantly different in both groups at the time of admission but improvement was significantly more in non- alcoholic group after two weeks (p<.05) and after six months (p<.01).There was significant difference serum BDNF levels at admission, after two weeks and after six months **(Table 2).** Improvement in scores was better in non- alcoholic stroke patients. Alcohol is a significant risk factor for poor outcome after stroke (F (2.5), p=.023). Other risk factors were Hypertension (F (4.35), p=.001), Hypercholesterolemia (F(26.38), p=.001), both DM+HTN (F (2.22), p=.036). We observed least levels of BDNF in alcoholics at admission and after six months.

Discussion

In our study patients had a history of moderate to severe alcohol consumption. Patients with the history of alcohol consumption exhibited recovery slower than the patients without alcohol consumption. On comparing mean BDNF values in both groups we found that patients with alcohol consumption had lower BDNF levels. This may be the cause of slow recovery and slow neural regeneration, synaptogenesis, angiogenesis and collectively neuroplasticity.

There was poor improvement in FIM scores in alcoholic stroke patients. Studies have proven that alcohol consumption leads to neuropathy. It is estimated that neuropathy occurs in 10% of chronic alcoholics. The most common type of neuropathy is progressive sensory axonal neuropathy [14-20]. Pain and dysaesthesia are common. As the neuropathy progresses motor weakness and muscle atrophy develop in a length dependent

Table 1 Socio- demographic factor, coexisting medical condition and baseline values of subjects.

Variables	Group 1 (Alcoholic) n=48	Group 2 (Non- alcoholic) n=160	p- value
Age (Years)	56.29 (11.06)	57.42 (10.35)	.79[a]
Sex (female/male)	0/48	40/120	<.05[a*]
Side affected (left/right) (n)	29/19	108/52	<.05[a*]
Type (ischemic/hemorrhagic) (n)	34/14	129/31	<.05[a*]
MCA stroke (n)	45	151	<.05[a*]
PCA stroke (n)	1	2	.92[a]
ACA stroke (n)	2	7	..69[a]
Hemianopia	1	3	.98[a]
Neglect	0	1	--
Hypertensive (HTN) (%)	80	70	.89[a]
Diabetic (DM) (%)	50	41	.92[a]
Both DM+HTN (%)	25	23	.23[a]
Dyslipidemia (%)	29	17	.04[a]
Smoking (%)	42	33	.32[a]
GCS (SD)	14.75 (0.21)	14.88 (.41)	.837[b]
NIHSS (SD)	9.46 (5.17)	8.03 (4.14)	.941[b]
ICH (Range)	2 (1-3)	1.5 (0-3)	.632[b]
mRS (SD)	3.45 (0.75)	3.66 (.895)	.850[b]
Cholesterol (SD)	178.47 (47.76)	157.00 (55.74)	.434[b]
Triglyceride (SD)	157.00 (55.74)	178.47 (47.76)	.434[b]
HDL (SD)	46.75 (13.45)	40.58 (9.43)	.280[b]
LDL (SD)	95.75 (40.97)	115.95 (43.05)	.400[b]
VLDL (SD)	15.50 (8.38)	19.00 (13.04)	.616[b]

GCS=Glasgow Coma Scale, NIHSS=National Institute of Health Stroke Scale, MRS=Modified Rankin Scale, HDL=High density lipoprotein, LDL=Low density lipoprotein, VLDL=Very low density lipoprotein, MCA=Middle cerebral artery, PCA=posterior cerebral artery, ACA=anterior cerebral artery. a=chi- square test, b=independent t- test, *=p<.05

Table 2 Functional Independence Measure (FIM) scores and serum Brain Derived Neurotrophic Factor level (BDNF) levels group 1 and 2.

Variables	Group 1 n=48 (Mean ± SD)	Group 2 n=160 (Mean ± SD)	p- value	95% CI	
				Lower	Upper
FIM (18-126)					
Admission	34.66 ± 9.81	39.48 ± 19.30	.562	-7.52	4.61
2 Weeks	60.33 ± 15.31	68.24 ± 20.29	.030*	-15.46	-.499
6 Months	96.00 ± 13.00	122.24 ± 9.6	.001**	-27.82	-17.64
S. BDNF (ng/ml)					
Admission	8.51 ± 4.26	10.34 ± 3.96	.006**	-3.93	-.682
2 Weeks	9.83 ± 3.14	11.13 ± 3.96	.025*	-3.06	-024
6 Months	8.80 ± .669	14.77 ± 2.88	.001**	-9.01	-4.44

Abbreviation: SD=Standard deviation, n=no. of cases, CI=confidence interval, BDNF=Brain Derived Neurotrophic Factor, FIM=Functional Independence Measure, *=p value <.05,**=p value <.01

manner. In alcoholics acute neuropathy resembling GB syndrome is typically painful and often associated with malnutrition and hepatic dysfunction. It differs from GB syndrome by normal CSF, and absence of demyelinating features on nerve conduction study. Sural nerve biopsy shows loss of large and small fibers without any demyelination or inflammation [21,22]. We also noticed complaints of pain, numbness and tingling in extremities in subjects with heavy alcohol intake and chronic alcoholics. In such patients BDNF level was very low at the time of admission. We also observed little recovery after two weeks in such patients **(Table 2).**

Patients with the history of alcohol consumption had lower BDNF levels as compared to non- alcoholic stroke patients. The improvement was not significant at two weeks in patients with alcohol consumption. Our results are supported by the findings that growth factors, long studied for their involvement in neuronal development and plasticity, also regulate responses to drugs abuse, including alcohol [23]. The study suggests interaction between the Brain-Derived Neurotrophic Factor (BDNF) and alcohol. Specifically, described studies in rodent models suggest that moderate consumption of alcohol increases BDNF levels in the dorsal striatum, which in turn act to suppress alcohol intake by activating a Mitogen-Activated Protein Kinase (MAPK)-dependent genomic mechanism. In another study alcohol intake suppressed BDNF expression, and resulted in the decrease of its downstream molecules, pERK1/2 and Bcl-2, in the hippocampus.

Alcohol intake may lead to a depressed-like state with reduced hippocampal cell proliferation through inhibition of the BDNF-ERK signaling pathway [24].

In a recent study it has been stated that no alcohol consumption improves health [25]. In our study, patients with history of alcohol consumption were having lower BDNF. We also observed that the patients, who were heavy alcoholics, had other comorbidities. In most of the patients other health issues such as liver, kidney and cardiac dysfunction was the common comorbidities and recurrent stroke was noted in some patients within one year. Results in our study bend the conclusion towards better improvement in non-alcoholic stroke patients. We can say that alcohol consumption deteriorates the progress of stroke recovery.

Limitation in our study was that other neurotrophins such as vascular endothelial growth factor and nerve growth factors should also be assessed to conclude that alcohol abuse is the cause of slow neurogenesis, angiogenesis and synaptogenesis. Another limitation was that alcohol abuse also causes cardiac and liver dysfunctions. With the improvement in BDNF levels, the cardiac and liver function tests should also be done. Patients should be followed up for more than six months.

Conclusion

The results of our study suggest that alcohol consumption impedes stroke recovery. So, intravenous BDNF may be tried for better recovery in alcoholic stroke patients. Intensive and prolonged rehabilitation should be implemented in such patients for complete recovery.

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References

1 Global status report on alcohol and health (2014) World Health Organization.

2 Baan R, Straif K, Grosse Y, Secretan B, Ghissassi EL, et al. (2007) Carcinogenicity of alcoholic beverages. Lancet Oncol 8: 292-293.

3 Shield KD, Parry C and Rehm J (2013) Chronic diseases and conditions related to alcohol use. Alcohol Res 35: 155-173.

4 Neuroscience of psychoactive substance use and dependence (2014) World Health Organization.

5 Sacks JJ, Roeber J, Bouchery EE, Gonzales K, Chaloupka FJ, et al. (2006) State costs of excessive alcohol consumption. Am J Prev Med 45: 474-485.

6 Anderson P (2005) Drug and alcohol policy at the global level. Drug Alcohol Rev. 25: 485-487.

7 Day CP, James OF, Brown AS, Bennett MK, Fleming IN and Yeaman SJ (1993)The activity of the metabolic form of hepatic phosphatidate phosphohydrolase correlates with the severity of alcoholic fatty liver in human beings. Hepatology. 18: 832-838.

8 Kiechl S, Willeit J, Rungger G, Egger G, Oberhollenzer F, et al. (1998) Alcohol consumption and atherosclerosis: What is the relation? Prospective results from the Bruneck Study. Stroke 29: 900-907.

9 Hodges DL, Kumar VN, Redford JB (1986) Effects of alcohol on bone, muscle and nerve. Am Fam Physician 34: 149-156.

10 Hohlfeld R (2008) Neurotrophic cross-talk between the nervous and immune systems: Relevance for repair strategies in multiple sclerosis? J Neurol Sci 265: 93-96.

11 Huang EJ, Reichardt LF (2001) Neurotrophins: Roles in neuronal development and function. Annu Rev Neurosci 24: 677-736.

12 Pikula A, Beiser AS, Chen TC, Preis SR, Vorgias D, et al. (2013) Serum brain-derived neurotrophic factor and vascular endothelial growth factor levels are associated with risk of stroke and vascular brain injury: Framingham Study. Stroke 44: 2768-2775.

13 Lasek-Bal A, Jedrzejowska-Szypulka H, Rozycka J, Bal W, Holecki M, et al. (2015) Low concentration of BDNF in the acute phase of ischemic stroke as a factor in poor prognosis in terms of functional Status of Patients. Med Sci Monit 21: 3900-3905.

14 Chopra K, Tiwari V (2012) Alcoholic neuropathy: Possible mechanisms and future treatment possibilities. Br J Clin Pharmacol 73: 348-362.

15 Narita M, Miyoshi K, Narita M, Suzuki T (2007) Involvement of microglia in the ethanol-induced neuropathic pain-like state in the rat. Neurosci Lett 414: 21-25.

16 Miyoshi K, Narita M, Takatsu M, Suzuki T (2007) mGlu5 receptor and protein kinase C implicated in the development and induction of neuropathic pain following chronic ethanol consumption. Eur J Pharmacol 562: 208-211.

17 Dina OA, Barletta J, Chen X, Mutero A, Martin A, et al. (2000) Key role for the epsilon isoform of protein kinase C in painful alcoholic neuropathy in the rat. J Neurosci 20: 8614-8619.

18 Gianoulakis C, Dai X, Brown T (2003) Effect of chronic alcohol consumption on the activity of the hypothalamic-pituitary-adrenal axis and pituitary beta-endorphin as a function of alcohol intake, age, and gender. Alcohol Clin Exp Res 27: 410-423.

19 Thayer JF, Hall M, Sollers JJ, Fischer JE (2006) Alcohol use, urinary cortisol, and heart rate variability in apparently healthy men: Evidence for impaired inhibitory control of the HPA axis in heavy drinkers. Int J Psychophysiol 59: 244-250.

20 Walter M, Gerhard U, Gerlach M, Weijers HG, Boening J, et al. (2006) Cortisol concentrations, stress-coping styles after withdrawal and long-term abstinence in alcohol dependence. Addict Biol 11: 157-162.

21 Wöhrle JC, Spengos K, Stenke W, Goebel HH, Hennerici M (1998) Alcohol-related acute axonal polyneuropathy: A differential diagnosis of Guillain-Barré syndrome. Arch Neurol 55: 1329- 1334.

22 Misra UK and Kalita J. (2009) Toxic neuropathies. Neurol India 57: 697-705.

23 Logrip ML, Barak S, Warnault V, Ron D (2015) Corticostriatal BDNF and alcohol addiction. Brain Res 1628: 60-67.

24 Kim JE, Ji SE, Seo JH, Lee MH , Cho S , Pak YK , Seo TB and CJ K. Alcohol exposure induces depression-like behavior by decreasing hippocampal neuronal proliferation through inhibition of the BDNF-ERK pathway in gerbils. Animal Cells and Systems 2012; 16: 190- 197.

25 Burton R, Sheron N (2018) No level of alcohol consumption improves health. Lancet 392: 987-988.