http://www.banglajol.info/index.php/JNINB

Original Article

DOI: http://dx.doi.org/10.3329/jninb.v4i2.38921

Journal of National Institute of Neurosciences Bangladesh,
July 2018, Vol. 4, No. 2, pp: 92-96

ISSN (Online) 2518-6612
ISSN (Print) 2410-8030

Single Photon Emission Computed Tomographic (SPECT) Study in Writer's Cramp Patients

Sharif Uddin Khan[1], Kazi Mohibur Rahman[2], ATM Hasibul Hasan[3], Anisul Hoque[4], AKM Anwar Ullah[5], Quazi Deen Mohammad[6]

[1]Associate Professor, Department of Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [2]Associate Professor, Department of Interventional Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [3]Registrar (Neurology), National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [4]Professor & Former Chairman, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [5]Professor & Former Chairman, Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [6]Director & Professor of Neurology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh

[**Received:** 2 March 2018; **Revised on:** 10 April 2018; **Accepted on:** 22 May 2018; **Published on:** 1 July 2018]

Abstract

Background: Writer's cramp is probably related to abnormal functioning of basal ganglia. But the actual mechanism is not known. **Objective:** The purpose of the present study was to evaluate the functional association of writer's cramp with basal ganglia through SPECT study. **Methodology:** This prospective case control study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka and institute of nuclear medicine (INM), Dhaka from July 2001 to June 2003 to understand the basic pathophysiology of writer's cramp by SPECT study and to compare the perfusion difference of basal ganglia between writer's cramp and non-writer's cramp group. A total of 20 respondents consisting of 10 in each group of writer's cramp and non-writer's cramp group as cases and controls respectively were enlisted by simple random method. Both the group of respondents underwent Tc^{99m} HMPAO SPECT study during rest and writing period. **Result:** Out of 10 cases male patients were nine (90%) and female patient was one (10%) with male female ratio 9:1. Majority of patients presented third to fifth decades of which maximum (30%) were from 30-34 age group. Total six (60%) patients had simple writer's cramp next three (30%) progressive writer's cramp and one with dystonic variety. Maximum writer's cramp patients were associated with great deal of writing (teacher, student, clerk, banker) and or performed repetitive hand movement (computer operator) from the point of occupational distribution. The perfusion difference of basal ganglia of both writer's cramp and non-writer's cramp group was seen by Tc99m HMPAO SPECT study during rest and writing period. First visual analysis of the scans by an expert nuclear medicine specialist showed no difference and then quantification of perfusion difference of basal ganglia by using SIEMENS macro programming environment (MPE) software showed no significant perfusion difference of basal ganglia between case and control group both during rest and writing period. In addition it was found highly significant perfusion difference (P=0.000321) separately in controls between left side and right side comparison during rest and significant difference (P=0.03) in writing and also significant in right side (P=0.022) during comparison of rest and writing period. The study also showed a significant perfusion difference (P=0.01) in cases between left and right comparison during writing and also significant perfusion difference (P=0.018) was found in rest and writing comparison of left side in writer's cramp patients. **Conclusion:** There is no abnormality in basal ganglia perfusion pattern among the writer's cramp patient. *[Journal of National Institute of Neurosciences Bangladesh, 2018;4(2): 92-96]*

Keywords: Writer's cramp; basal ganglia; Single Photon Emission Computed Tomographic; SPECT

Correspondence: Dr. ATM Hasibul Hasan, Registrar (Neurology), National Institute of Neurosciences & Hospital, Sher-E-Bangla Nagar, Agargaon, Dhaka-1207, Bangladesh; Cell no.: +8801763498663; Email: parag007us@gmail.com

Conflict of interest: There is no conflict of interest relevant to this paper to disclose.

Funding agency: This research project was not funded by any group or any institution.

Contribution to authors: SU Khan is the main researcher of this study. He collected the data and wrote whole part of the manuscript and KM Rahman helped in planning the research. ATMH Hasan helped to collect the data and help in statistical analysis of data. A Hoque, AKMA Ullah and QD Mohammad guided us and gave a support to collect data and write the manuscript.

How to cite this article: Khan SU, Rahman KM, Hasan ATMH, Hoque A, Ullah AKMA, Mohammad QD. Single Photon Emission Computed Tomographic (SPECT) Study in Writer's Cramp Patients. J Natl Inst Neurosci Bangladesh, 2018;4(2): 92-96

Introduction

Initial description of Writer's cramp was given in nineteenth century in medical books; where it was known as Scrivener's palsy. It is a form of task specific focal dystonia of the hand. Dystonia is an involuntary sustained muscle contraction causing twisting movements and abnormal postures[1]. Writer's cramp is the most common dystonia occurring in the setting of repetitive movement disorders. Writer's cramp is believed to be due to abnormal functioning of the basal ganglia. What goes wrong in the basal ganglia is still unknown. An imbalance of dopamine, a neurotransmitter in the basal ganglia, may underlie several different forms of dystonia but much more research needs to be done for a better understanding of the brain mechanisms involved with dystonia. The advent of high-resolution neuroimaging, particularly single photon emission computed tomography (SPECT) has greatly enhanced our ability to identify the underlying causes if any, incase of writer's cramp patients. The sensitivity and specificity of SPECT is higher than any other modalities of imaging like computed tomography (CT) and magnetic resonance imaging (MRI). Although positron emission tomography (PET) has better detection capacity both in respect of sensitivity and specificity but it's overall cost is higher than SPECT. As a result its use is not wide spread. In patients with writer's cramp, PET studies during writing showed a reduced activation of contralateral primary motor cortex and enhanced activation of the frontal association cortex[2]. Additionally an increased activation of the left thalamus and the ipsilateral cerebellum more than the contra lateral cerebellum were found[3].

One of the major reasons for the growing interest in SPECT is that it represents a less expensive functional neuroimaging technique[4]. SPECT cannot measure regional cerebral metabolism, but it does provide a qualitative estimate of regional cerebral blood flow (r CBF), which in many neurologic disorder is tightly coupled with brain metabolism. Thus SPECT provides functional information not available by conventional CT or MRI[5]. SPECT study in writer's cramp patient in Bangladesh can give us new information about the pathophysiology of the condition. Therefore this present study was undertaken to evaluate the functional association of writer's cramp with basal ganglia through SPECT study.

Methodology

This study was a prospective case-control study, conducted in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, and Institute of Nuclear Medicine (INM), Dhaka from July 2001 to June 2003. All the clinically suspected cases of writer's cramp patients aged between 18 to 50 years with no abnormality in CT scan or MRI were included in the study. The Department of Neurology, BSMMU, maintains different types of outdoor services and clinics. Professors, Associate professors, Assistant professors and medical officers attend the outpatient department according to fixed schedule. There are also some specialized clinics for specific diseases (e.g. Epilepsy, Headache, stroke, movement disorders, degenerative disorders etc.) giving services to the people with utmost care. Every Sunday, there was movement disorders clinic in the Neurology outpatient department (OPD). Proper history and preliminary investigations were done here. Subsequently, these patients attended indoor clinic every Tuesday, where, in presence of senior neurologists, we again examined the patients and after thorough discussion and necessary investigations, diagnosis and classification were made. More over subjects were also collected from fortnightly-arranged clinical meeting of neuroscience conducted by Society of Neuroscience in the Neurology department. We excluded patients with H/O action or rest tremor, rigidity, bradykinesia, H/O stroke or other neurologic deficit, any abnormality in thyroid function or serum copper/ ceruloplasmin or urinary copper level, any patient with depression. The purpose of the study, side effects and contraindications of radioactive substance (Tc^{99m} HMPAO) were explained to each subject and attendant before entry into the study. Same numbers of (i.e. 10) age-matched controls were included in the study after proper explanation of purpose of the study, side effects and contraindication of radioactive substance (TC^{99m} HMPAO). Informed written consents were taken from both cases and controls. All the relevant information were recorded in a predesigned questionnaire and data sheet. Total 10 cases and 10 controls comprised age-matched were done SPECT scan using identical protocol during rest and writing. We used Tc^{99m} HMPAO (hexamethylpropyl-eneamineoxime). This was a functional study and blood flow was seen. The brain perfusion is proportional to blood flow and higher blood flow is shown as higher concentration of tracer and decreased blood flow on the other hand results in decreased concentration in brain. In a quiet room patients begun to write for at least 1 – 2 minutes till problem started. Then TC^{99m} HMPAO was

slowly injected and scan was done. Siemens' Orbiter SPECT double-headed gamma camera was used. A total number of 128 views were taken with 30-seconds interval. The camera was rotated 360 degrees around the patient's head. A total of 40 minutes required to complete a study. The images were acquired and processed in Computer. All the slices were reconstructed in coronal, sagital and transverse plane by filtered back-projection method. An experienced Nuclear Medicine physician who was blind to all clinical details visually analyzed the SPECT scans. Finally after collection of all the data statistical analysis was done using SPSS version 7.

Results

Observations of the study were analyzed by comparison among the writer's cramp and non-writer's cramp group to detect whether there was any change of perfusion in basal ganglia.

Demographic information of both groups: Among the 10 writer's cramp age in years (Mean ± SD) were 33.8 ± 9.70 and range between 20 to 50 years and highest proportion of them (30%) were in the 30 – 34 age group and in non-writer's cramp, ages (Mean ± SD) are 35.1 ± 2.96 where maximum 6 (60%) of non-writer's cramp are in 35 – 39 years age group. There was no significant relationship between the mean ages of the two groups (P>0.05).

Table 1: Age Distribution of writer's cramp and non-writer's cramp (n=10)

Age Groups	Writer's cramp	Non-writer's cramp
20 to 24 Years	2(20.0%)	0(0.0%)
25 to 29 Years	0(0.0%)	0(0.0%)
30 to 34 Years	3(30.0%)	3(30.0%)
35 to 39 Years	2(20.0%)	6(60.0%)
40 to 44 Years	1(10.0%)	1(10.0%)
45 to 49 Years	2(20.0%)	0(0.0%)
Total	**10(100.0%)**	**10(100.0%)**
Mean±SD	33.8±9.70	35.1±2.96

Among the writer's cramp 90.0% cases were male and 10.0% cases were female but in non-writer's cramp (n=10) no male female variation was maintained (Figure I).

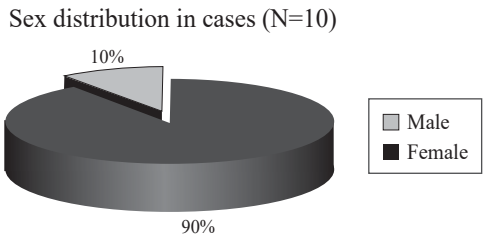

Figure I: showing sex distribution among writer's cramp patients (n=10), M: F=9:1

The writer's cramp were comprised of 3 different types of writer's cramp based on Sheehy Marsden's typing of writer's cramp and showed simple variety of writer's cramp is predominant 6(60%) followed by progressive 3(30%) and 1(10%) in Dystonic subsets (Table 2).

Table 2: Distribution of types of writer's cramp in writer's cramp (N=10)

Types	Frequency	Percent
Simple	6	60.0
Progressive	3	30.0
Dystonic	1	10.0
Total	**10**	**100.0**

Family history showed positive relation in only 1(10%) out of 10 writer's cramp patients (Table 3).

Table 3: Family history of writer's cramp in writer's cramp (N=10)

Family history	Frequency	Percent
Negative	9	90.0
Positive	1	10.0
Total	**10**	**100.0**

The writer's cramp was comprised of 6 occupational groups. Among them occupational distribution of writer's cramp where maximum cases of writer's cramp were associated with great deal of writing 90.0% like student 3(30%) maximum followed by chronologically 2(20%) in teacher, 2(20%) in clerk, 1(10%) in banker or repetitive hand movement like computer operator 1(10%) (Table 4).

Table 4: Occupational Distribution among Writer's Cramp (n=10)

Occupation	Frequency	Percent
Teacher	2	20.0
Student	3	30.0
Clerk	2	20.0
Banker	1	10.0
Driver	1	10.0
Computer operator	1	10.0
Total	**10**	**100.0**

Perfusion pattern of basal ganglia in non-writer's cramp group (left and right side during rest and writing): Visual analysis of scan of non-writer's cramp show no obvious difference in perfusion pattern between right and left hemisphere obtained during rest

and writing. But after computer quantification analysis there is highly significant difference (P=0.000321) of perfusion between right and left side of non-writer's cramp during rest and also there is significant difference of perfusion (P=0.03) during writing between left and right side in non-writer's cramp. But there is no significant difference of perfusion (P=0.629) between rest and writing in left side of non-writer's cramp. And there is significant difference (P=0.022) of perfusion between rest and writing in right side in non-writer's cramp.

Perfusion pattern of basal ganglia in writer's cramp group (left and right side during rest and writing): Visual analysis of scan of writer's cramp show no obvious difference in perfusion pattern between right and left hemisphere obtained during rest and writing. But after computer quantification analysis there is no significant difference (P=0.135) of perfusion between right and left side of writer's cramp during rest but there is significant difference of perfusion (P=0.01) during writing between left and right side in writer's cramp. There is significant difference of perfusion (P=0.018) between rest and writing in left side of writer's cramp but there is no significant difference (P=0.58) of perfusion between rest and writing in right side in writer's cramp.

Discussion

This was a prospective case control study where ten cases and ten controls were included in the study. The study population was divided into two separate groups of equal number of respondents- one was case group who had writer's cramp and another one is control group having no writer's cramp. The study was carried out to compare whether or not any change of perfusion in basal ganglia during rest and writing between two groups. Tc^{99m} HMPAO SPECT study was done to see the perfusion pattern of both groups.

In this study all the writer's cramp patients were of 20-50 years age group. Masden CD et al[4] showed peak incidents of writer's cramp between third to fifth decades. This observation supports our series. Sex distribution of present series showed that out of ten writer's cramp patients, nine (90%) were male and one (10%) was female. This figure did not correlate with epidemiological study of dystonia in Europe- a collaborative study where they showed male affected slightly higher with male female ratio of 1.3:1. One possible explanation for this discrepancy in male female ratio may be due to small number of writer's cramp patient.

The most common types of writer's cramp were simple type (60%) in this study that had similarity with the study of Sheehy and Masden[5]. In this study family history was positive in 10% of writer's cramp patients. But Sheehy et al[5] showed approximately 5% of patients with writer's cramp was related with positive family history of a similar condition. That is non consistent to our study. In this present study maximum writer's cramp was associated with great deal of writing person like teacher, student, clerk which is consistent with Harrington's study[6].

In this present study there was no significant perfusion difference of basal ganglia between writer's cramp and non-writer's cramp group in the left side (P=0.851) during writing and also in the right side (P=0.671). The study also showed that no significant difference of perfusion between two groups in the left side (P=0.123) during rest and also in the right side (P=0.382). Horstink et al[7] showed that the striatal dopaminergic system is involved in writer's cramp and those patients had a significantly lower level of striatal [1231] IBZM binding than controls. There observation is contrary to this study. In a functional MRI study Preibisch et al[8] observed healthy subjects showed a significant activation of the ipsilateral dentate nucleus, contralateral cerebeller hemisphere, contralateral primary sensory motor cortex and contralateral precentral gyrus during writing. Patients with writer's cramp significantly greater activation of the ipsilateral cerebellar hemisphere than controls. Also the activation in the primary sensory motor cortex extended further caudaly and anteriorly towards the premotor area. Activation was observed in the thalamus during writing only among the patients. There results indicated an increased basal ganglia output via the thalamus to the motor and premotor cortical areas in dystonia patients and support the notion of disinhibition of the motor cortex leading to concentration and dystonic postures. There observation was not supportive to our study as because region of interest (ROI) was basal ganglia. Moreover, researchers used statistical parametric mapping (SPM96) software that gave them more precise analysis of perfusion changes that was not in our study. In another PET study patients with dystonia revealed hypometabolism of glucose in the basal ganglia, thalamus and prefrontal association cortices[9] and hypoactivity of regional cerebral blood flow in the primary sensory motor cortex (SMC) and supplementary motor area (SMA) to various sensory motor tasks[10]. That was also contrary to this observation. Oga et al[11] evaluated the cortical activities

associated with voluntary muscle contraction and relaxation separately in patients with writer's cramp using event related functional MRI. The impaired cortical activation of SMC and SMA by various motor tasks in patients with dystonia has been shown by previous PET studies[10]. But both the observation were contrary to present study, possibly due to limitation of software used to see the perfusion pattern of region of interest. Mink et al[12] showed basal ganglia act broadly to inhibit the competing motor mechanisms that would otherwise interfere with the desired movement that was not in favour of this observation. On the other hand present study showed a highly significant perfusion difference (P value=0.000321) between right and left side of non-writer's group during rest and also significant difference of perfusion (P value=0.03) during writing between left and right side in controls. No study was found similarity or dissimilarity with this observation. In the present study there was significant difference of perfusion (P value=0.01) during writing between left and right side in writer's cramp group. There was also significant difference of perfusion (P value=0.018) between rest and writing in the left side of writer's cramp group. No study in favour of this observation was found. No relation of significant perfusion difference of basal ganglia was found between writer's cramp and non-writer's cramp group in this study that was consistent with clinical presentation. Tc^{99m} HMPAO SPECT was done in our study where we used SIEMENS macro programming environment (MPE) software for quantification that could not quantify very small fraction of perfusion changes that would be possible by latest software like statistical parametric mapping-2 (SPM-2).

Limitations included EMG study of writer's cramp patient. We took those slices for quantification that cover mostly at the level of basal ganglia by a experienced nuclear medicine expert. We cannot eliminate the possibility of biasness during selection of slices covering basal ganglia for quantification. Moreover the study had insignificant statistical value that might be due to small group size. It cannot be determined from the study why there was significant perfusion difference of left and right side comparison in non-writer's cramp group during rest and writing and also significant perfusion difference during rest and writing in the right side of the same group. Same difficulty prevailed to explain in writer's cramp group during writing as well as comparison of rest and writing in the left side of writer's group.

Conclusion

In this study basal ganglia perfusion pattern was found to have no abnormality in writer's cramp patient. Maximum writer's cramp of writer's cramp are associated with great deal of writing like teacher, student, clerk, banker patients or perform repetitive hand movement like computer operator. Additional in depth research is needed to determine the pathophysiology of writer's cramp patient.

References

1. Fahn S, Marsden CD, Calne DB. Classification and investigation of dystonia. In: Marsden CD, Fahn S, editors. Movement disorders 2. London: Butterworths; 1987. p. 332–58.
2. Odergren T, Stone Elander S, Ingvar M. Cerebral and cerebellar activation in correlation to the action induced dystonia in writer's cramp. Mov. Disord 1998,13:497-508.
3. Rao SM, Binder JR, Bandettini PA, Hammeke TA, Yetkin FZ, Jesmanowickz A, Lisk LM, Morris GL, Meuller WM, Estkowski LD et al. Functional magnetic resonance imaging of complex human movements. Neurology 1993; 43:2311-18.
4. Masden Jc, Heertum R, Kleiman A. Early SPECT in mild hand trauma: a controlled study. Neurology 1994; 44:177-81.
5. Sheehy MP, Marsden CD, Writer's cramp-a focal dystonia. Brain 1982; 105:461-80
6. Harrington R C, Wieck A, Marks IM, Marsden C D. Writers cramp: not associated with anxiety. Mov Disord 1988; 3: 195-200.
7. Horstink CA, Praamstra, P. Horstink WM, Berger, H.J, Booij J, Van Royen EAl. Low striatal D2 receptor binding as assessed by [1231] IBZM SPECT in patients with writer's cramp. JNNP 1997; 62(6): 672-6.
8. Preibisch C, Berg D, Hofmann E, Solymosi L, Naumann M. Cerebral activation pattern in patients with writer's cramp a functional magnetic resonance imaging study. Journal of Neurology 2001; 248:10-17.
9. Karbe H, Holthoff VA, Rudolf J, Herholz K, Keiss WD. Positron emission tomography demonstrates frontal cortex and basal ganglia hypometabolism in dystonia. Neurology 1992; 42:1540 – 4.
10. Ceballos-Baumann AO, Passingham RD, Warner T, Playford ED, Marsden CD, Brook DJ. Overactive free frontal and under active motor cortical areas in idiopathic dystonia. Ann Neurol 1995; 37:363-72.
11. Oga T, Honda M, Toma K, Murase N, Okada T, Hanakawa T, Sawamoto N, Nagamine T, Konishi J, Fukuyama H, Kaji R, Shibasaki H.. Abnormal cortical mechanism of voluntary muscle relaxation in patients with writer's cramp a functional MRI studies. Brain 2002; 125: 895-03.
12. Mink JW. The basal ganglia: focused selection and inhibition of competing motor programs. Prog Neurobiol 1996; 50:381-25