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TRANSCRANIAL DOPPLER STUDY OF INTRACRANIAL ARTERIAL RESISTANCE AND VASOREACTIVITY IN TYPE 2 DM WITH STROKE.

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ABSTRACT

BACKGROUND : The pulsatility index reflects the vascular resistance of intracranial arteries and could therefore be used as an estimate of the severity of vascular damage.similarly T2DM leading to decreased vasomotor reactivity and causing complications like stroke .

AIM : The present study aimed to examine the influence of type 2 diabetes mellitus on intracranial vascular resistance in patients with a previous stroke and to assess vasomotor reactivity by breath holding.

MATERIAL AND METHODS : Transcranial doppler investigations were performed in 102 patients with previous stroke (40 with T2DM, 62 T2DM), at least 3 months after stroke occurred. Gosling's pulsatility index was calculated. The maximum pulsatility suggestive of more pronounced damage. Baseline MCA MFV obtained before and after 30 sec of breath holding and breath holding index calculated.

RESULTS : Diabetic patients had a significantly higher pulsatility index than non-diabetic patients in all intracranial arteries. The maximal pulsatility index was also significantly higher in diabetics than in non-diabetics (1.29 +/- 0.37 vs. 1.05 +/- 0.20; $p < 0.0001$). Among 40 with T2DM and stroke 32 had BHI less than1.5 than without T2DM in which out of 62 only 16 had BHI less than 1.5.

CONCLUSIONS: Diabetic patients with previous stroke have a higher pulsatility index than non-diabetic patients with previous strokes, indicating a higher increase in intracranial arterial resistance. Patients with T2DM had lesser BHI index than without T2DM with stroke suggesting lesser vasomotor reactivity in T2DM.

KEYWORDS :

INTRODUCTION

Transcranial Doppler (TCD), first experimented and came in use in the year 1982.(1) It is a basically ultrasound (US) which noninvasively monitors flow of blood across the intracranial vessels like middle cerebral artery (MCA),anterior cerebral artery (ACA) and posterior cerebral artery (PCA) which uses a low-frequency (≤2 MHz) transducer probe to send sonic waves to record flow in the cerebral arteries through relatively thin bone windows.(2)

TCD allows dynamic monitoring of cerebral blood flow velocity (CBF-V) and vessel pulsatility over extended time periods with a high temporal resolution The technique is dependent on operator and have subjective variations in recordings, which is limitation for its utility. It is also very hard to practice and very difficult to get three dimensional views and understanding of cerebrovascular anatomy necessary for competency.

Again approximately 10–20% of patients have poor transtemporal acoustic windows which further increases problem in mastering the procedure(3)..The pulsatility index reflects the vascular resistance of intracranial arteries and could therefore be used as an estimate of severity of vascular damage.

Pulsatility index (PI) –

It is the surrogate marker of cerebral flow resistance (or arterial stiffness) measure by subtracting End diastolic velocity (EDV) from Peak systolic velocity (PSV) and dividing it by Mean flow velocity (MFV).(1) PI is independent of angle of insonation and has no unit with an arbitrary value of more than 1.2 representing high blood flow resistance.

Mean blood flow velocity (MFV in cm/s) - It is the surrogate marker for cerebral blood flow. It is calculated by EDV plus one third of difference of PSV and EDV. MCA has the highest velocity among all major intracranial arteries. Decreased flow velocity in stroke may suggest cerebral hypoperfusion.

Similarly vasoreactivity which is the change in cerebral blood flow in response to a vasodilatory or vasoconstrictive stimulus can also be assesed with TCD by comparing breathholding index (BHI).(4)

Breath holding is one of the earliest method used to induce hypercapnia which causes progressive increase in PaCo2 with time.(5) It was first demonstrated by ***Ratnatunga et al*** in 1990 to demonstrate the risk of impending stroke in symptomatic carotid artery disease using TCD.

BHI is calculated as cited below :

BHI (%) = [(MFVapnea – MFVrest) / MFVrest × 30] × 100. (6)

Long time T2DM leads to loss of cerebral vasoreactivity which has been postulated as one of the reasons for diabetes related complications like ischaemic stroke; will be compared between diabetics and healthy individuals by obtaining breath holding index BHI.

AIMS AND OBJECTIVES

1. To study the influence of T2DM on intracranial arterial vascular resistance in patients with previous stroke with T2DM and without T2DM by PI.
2. To assess the use of TCD as screening tool for loss of vasoreactivity in long term diabetics and nondiabetics by comparing BHI.

METHODOLOGY (MATERIALS & METHODS)

This case control study done in tertiary hospital in madras medical college chennai over a period of 6 months.

Subjects : Transcranial Doppler performed in 102 patients in which 40 was with T2DM and 62 was without DM atleast 3 months after stroke occurred; Gossling's pulsatility index calculated in 40 cases and matched with controls with same age without diabetes .

Similarly vasoreactivity also compared in between the similar group by comparing BHI , in them observation only made in MCA to have uniformity and simplicity.

Inclusion Criterias :

40 cases with recently diagnosed type 2 DM with stroke has been taken along with 62 age matched control who are having stroke without T2DM within age range of 45-70 yrs with normal carotid artery doppler.

Exclusion Criterias :

1) Patients with comorbidities like hypertension and coronary heart

disease are excluded
2) Patients with severe MCA occlusion and carotid artery occlusion along with those having acute stroke within 3 months not been considered
3) Those who are not able to hold the breath for 30sec.and with cardiorespiratory ailments been excluded

Ultrasound investigation :
A color- coded 2.5 MHz phased-array probe transcranial duplex ultrasound was used in a standard transtemporal approach to analyse mean blood flow velocity (Vmean) and pulsatility index (PI) .The subjects were studied in the sitting position and recordings obtained from MCA,ACA,PCA,BA and vertebral arteries. Normal PI value range is between 0.5-1.19, any value of 1.2 and above taken as abnormal and comparison done between the groups.

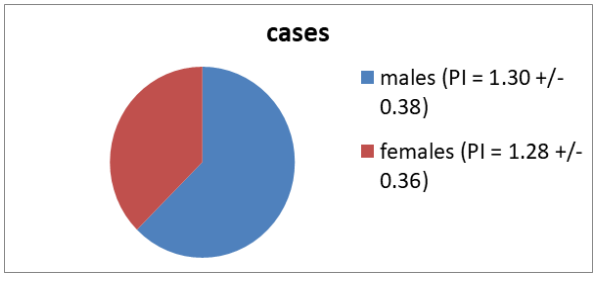
For vasoreactivity testing MCA mean velocity continuously monitored for around 3-5 minutes to obtain baseline values. Breath was held for 30 seconds and values 3 second before the release of breath were taken into consideration for Vmax calculation.

Breath holding index was calculated as percent of velocity increase from resting baseline values divided by breath holding time.

A descriptive study of ***Mousavi et al*** in 2005 has given normative values of BHI for women it is 0.918 +/- 0.4 and men 0.637 +/- 0.22 Hence an arbitary cut off value of 0.5 was taken for BHI and values less than 0.5 was taken as abnormal.

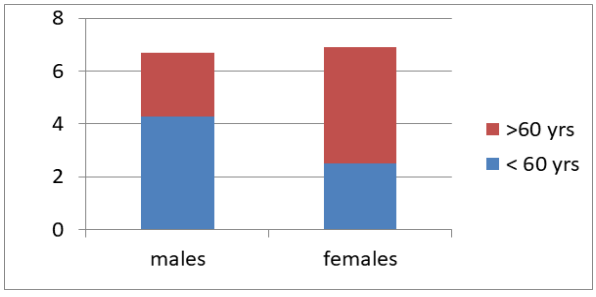
Statistic Methods
Descriptive data and results of measurements are presented as mean ± SD. Non-parametric data of differences in mean blood flow velocity (V mean) and PI were done using analysis of variance (ANOVA) and for with physiologic parameters Spearman rank correlation coefficient was used. SPSS software (version 22) was used for all statistical analysis and a p value of less than 0.05 was considered statistically significant.

RESULTS
Baseline characteristics :
Out of 40 cases males were 25 and females were 15 and no significant difference in PI found between males and females. PI in males found to be around (1.30+/- 0.38) and in females 1.28 +/- 0.36.



- These group further divided age wise into less than 60 yrs and more than 60 yrs .
- Males < 60yrs = 14, males >60 yrs = 11
- Females< 60 yrs = 5, females > 60 yrs = 10.
- PI in samples with age < 60 yrs found to be 1.24 +/- 0.27 and > 60 yrs 1.29 +/- 0.47 with (p= < 0.01).

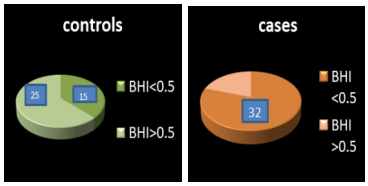
Thus indicating significant association between age and PI,as the age increases PI increases



•In diabetic patients PI found to be (1.29 +/- 0.37) vs (1.05 +/- 0.20) in non diabetics (p<0.01).

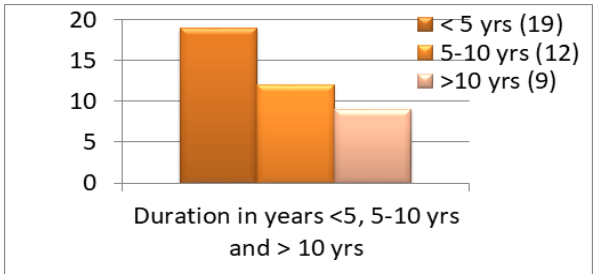
- Suggesting maximal PI was significantly higher in diabetic patients than in non diabetic patients.
- Thus in our analysis the presence of diabetes (p<0.01) and the age of patients (p<0.01) were the only factors significantly predicting maximal pulsatility index.
- 40 patients with T2DM and stroke matched with 40 age matched control , male 25 and females 15.

Among 40 with T2DM with stroke , 32 had BHI < 0.5 and in control group only 15 had BHI <0.5.



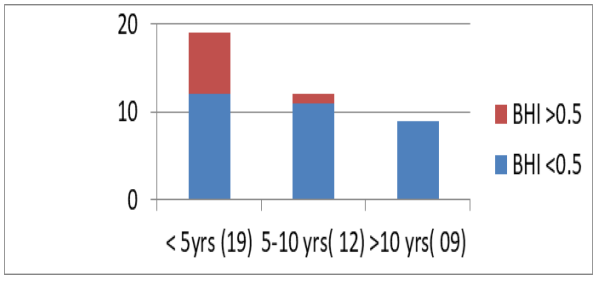
•In > 10 yrs T2DM group all 9 had BHI <0.5, in 5-10 yrs duration , 11 out of 12 had BHI < 0.5 and 12 out of 19 in < 5 yrs group.

According to statistical analysis BHI was significantly correlated with duration of diabetes (p=0.015)



2 linear relationships have been evaluated in this study i.e.

1) 32 out of 40 diabetics as compared to 15 out of 40 in non diabetics developed BHI < 0.5 (p<0.05)
2) As the duration of diabetes increased BHI significantly decreased (p<0.05)



DISCUSSION
In this study diabetics found to have more pulsatility index as compared to non- diabetics with stroke ;suggestive of more narrowing of caliber of intracerebral arteries may be due to more atherosclerotic changes and increase in resistance.in diabetic male it is found to be (1.30+/- 0.38) and in females found to be (1.28 +/- 0.36) which is nearly correlating with the studies previously done by Europian groups showing values slightly lower than our study i.e. (1.29+/-0.35) in males and (1.27+/-0.38) in females respectively.

Also those having age >60 yrs found to have high PI than those with age < 60 yrs and results were statistically significant showing as the age progresses intracranial arterial resistance increases correlating with the studies done **by Jeong et (6) and Europian study.**

This correlation may be due to atherosclerotic plaques and stiffness in the arteries due to age related degeneration but as diabetes leads to more atheroma formation and lipid deposition that may be the main reason of having high PI in diabetics than nondiabetics as age matched controls are used in this study.

According to one Europian study done by ***Tkac et al*** showed that presence of T2DM and age were the only factors significantly predicting the maximal pulsatility (7); showing similar results obtained in our study.

In this study, significant difference observed between BHI in samples with diabetics and nondiabetics(7). Also duration of diabetes affects the CVR, as the duration increases number of samples having low BHI found to be increased.(8)

Study done in 2013 by ***Vuletic V et al*** regarding impaired cerebral vasoreactivity in T2DM showed similar results as obtained in this study.(9)

Assesment of CVR can provide information regarding the reserve capacity of cerebral circulation,(10) that is possibility of vessels to adapt in response to systemic modification or brain metabolic activity requiring an increase or decrease in cerebral flow. Reduction of this property has been found in association with predisposing cerebrovascular disease.

CVR can be done by various methods like giving iv acetazolamide and other drugs but breath holding is the safest and noninvasive way of doing it as when we hold breath for 30 sec induced hypercapnia only causes vasodilatation and can be used as parameter for assessing vasomotor reactivity (10).

CONCLUSION

- Transcranial doppler is an important tool in assessing intracranial arterial resistance with measurement of Pulsatility Index and also in assessing CVR with the help of BHI.
- Diabetic patients with previous strokes have higher PI measured by TCD than non diabetic patients , indicating more severe damage to cerebral blood flow in diabetes mellitus.
- As the age increases PI increases and intraarterial resistance increases in T2DM with stroke.
- BHI is nonagressive,well tolerated,real time,reproducible screening method to study cerebral haemodynamics.
- BHI obtained from TCD monitoring showed that Diabetics have decreased CVR as compared to nondiabetics

As the age and duration of diabetes increases PI increases and CVR decreases .

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