Section: Cardiology

Original Research Article

A STUDY ON THE PREVALENCE OF REFLEX MEDIATED SYNCOPE IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Syncope is very common symptom presenting in day to day clinical practice. It causes includes cardiac causes, neurological causes, metabolic causes, psychiatric causes and neurally mediated reflex syncopal syndromes. I want to study the prevalence and role of various types of neutrally mediated syncope (neuro-cardiogenic or vasovagal syncope, carotid sinus syncope, situational syncope) as a cause of unexplained syncope. It is diagnosed on the basis of the results obtained from supine and standing blood pressure, carotid sinus massage and head-up tilt table test. I also want to see in this study if more patients of carotid sinus syndrome are detected if carotid sinus massage is done both before and after head up tilt table test

Materials and Methods: It is a prospective observational study with cross-sectional design in a single tertiary care centre with total of 150 patients. Face to face interview to obtain informed consent from the prospective group of patients. Then obtain data on age, sex, co morbid condition, results of blood pressure, carotid sinus massage and head-up tilt table test were recorded for further analysis.

Results: Total sample size was 150. After analyzing the study the age range of the study population was between 20 to 80 years age with mean age 61.2 ±11.5 years .Proportion of male to female was 56.7% :43.3% which was statistically not significant (p=0.102).Prevalence of neuro-cardiogenic cause of syncope was 42% (63 cases), carotid sinus syndrome was 9.3%(14 cases), cardiogenic cause 28% (42 cases), orthostatic hypotension was 4.7%(7 cases) and unknown cause of syncope 16%(24 cases). Reflex syncope which includes neuro cardiogenic syncope, orthostatic hypotension and carotid sinus syncope accounted for 56% (84 cases).Neuro-cardiogenic sub type showed Type 1 response in11.1%, Type 2A in 7.9%, Type 2B in 9.5% and Type 3 in 71.5%.Carotid sinus syndrome was diagnosed in 14 patients out of 150. While 12 patients were diagnosed before head up tilt test and 2 further patients were diagnosed when carotid sinus massage was done after head up tilt test .Orthostatic hypotension was detected in 4.7% patients (Total 7 patients) in the above study.
.In patients less than 65 years age neurocardiogenic cause accounted for54%, Carotid sinus syndrome accounted for 7%, Orthostatic hypotension for 6%, cardiogenic cause accounted for 14% and unknown was 19%.In patients with age≥ 65 years age neurocardiogenic syncope accounted for 29%, Carotid sinus syndrome 17%, Orthostatic hypotension accounted for 3%, Cardiogenic cause accounted for 44% and unknown in 11%. In age less than 65 years neurocardiogenic syncope accounted for 54%, Cardiogenic cause accounted for 14%, Orthostatic hypotension accounted for 6%, Carotid sinus syndrome 7% and unknown cause accounted for 19% of the cases. In age greater than equal to 65 years neurocardiogenic syncope accounted for 29%, Cardiogenic cause accounted for 44%, Orthostatic hypotension accounted for 3%.

Conclusion: Reflex mediated syncope is the most common cause of syncope in general. Reflex mediated syncope can be diagnosed reliably from typical history and with routine measurements of supine and standing blood pressure, carotid sinus massage and Head up tilt table test. however cardiogenic cause is also quite common and cardiogenic causes of syncope carries a graver prognosis so more vigilance is required in elderly. While performing carotid sinus massage it is better to perform it in standing position and preferably both before and after head up tilt table test as more cases of carotid sinus syndrome can be detected this way
Keywords: Reflex syncope, Head up tilt table test, carotid sinus massage.

INTRODUCTION

Syncope, a self-limited transient loss of consciousness and postural tone due to global cerebral hypoperfusion, is one of the common reason for hospital visits.[1] It leads to 3 % visits to emergency department and 6% of emergency hospital admission and 20 to 50% will experience one episode of syncope in their lifetime. Prevalence of syncope increases with age and it is more than 20% for older than 75 years.[2-4] Annual incidence is around 2% in those greater than 80 years. Syncope in elderly leads to significant morbidity and mortality.35% of syncopal episodes in elderly leads to injury and 2-year mortality rate is over 25%.[5] Older adults suffer from many chronic illness and are also on polypharmacy which contributes to the complexity of assessment and management of syncope in the elderly. Elderly also have altered cardiovascular structure and function. There are attenuated baroreceptor and autonomic reflexes, impaired adrenergic function, diastolic dysfunction and impaired ability to maintain intravascular volume due to decreased salt/water handling and renin-angiotensin-aldosterone level. This contributes to increased incidence and prevalence of syncope in elderly.

Transient loss of consciousness is an apparent loss of consciousness with an abrupt onset, short duration and spontaneous and complete recovery. It is usually determined by history taking. First there is loss of normal motor control in form of flaccidity or stiffness and postural control is lost so that patients falls if they are in upright position. Second normal responsiveness is lost. Third the patient experience amnesia for the event.

Review of Literature

A prospective study was conducted on consecutive patients with syncope who were referred to emergency departments of 11 general hospitals where strict adherence to guidelines were maintained. A diagnostic workup consistent with guidelines were maintained in 465/541 patients (86%). Definitive diagnosis was made in 98% patients: Neurally mediated syncope was most common cause 66%, orthostatic hypotension in 10%, primary arrhythmias in 11%, structural heart and cardiopulmonary disease in 5% and non-syncopal attacks in 6%. The initial evaluation (consisting history, physical examination and electrocardiogram) clinched the diagnosis in 50% of patients. Syncope was managed with hospitalisation in 255 of patients and it was required for other reasons in 13% cases. Apart from initial evaluation, a mean 1.9±1.1appropriate tests were performed in 193 cases and final diagnosis was reached in 182 cases (94%). The results of the study assess the current standard of syncope management in Europe as per the standard European guidelines.[1]

In Another study carotid sinus massage was done in 139 patients of whom 29 showed positive response. 18 that is 62% of these total 29 showed positive response when carotid sinus massage was done after the head-up tilt table test. The majority of positive patients were of the vasodepressor subtype. Head-up tilt table test was performed in 149 patients. Results were positive in 13 cases. Most common response was also vasodepressor type. Final conclusion was Carotid sinus syndrome was responsible for 20.8% of and neurocardiogenic syncope was responsible for 8.7% cases of unexplained syncope.

A study on 302 patients aged 71±11(range 38-98) years, were investigated with Carotid sinus massage. 74 patients (25%) had a positive response to Carotid sinus massage. Of them 50% was vasodepressor type and another 50% developed asystole. They performed carotid sinus massage in upright position. It was concluded that orthostatic hypotension, neurocardiogenic syncope and Carotid sinus hypersensitivity often coexists in older patients with syncope.

In the offspring cohort of the Framingham study (3491 subjects, 1845 women, mean age 55 years, range 26 to 84 years) the cumulative incidence of syncope in 4 years follow up was 3%.18In the Framingham report Reflex syncope (labelled as vasovagal syncope in the report) was the most common cause of syncope (21.2%), followed by cardiac syncope with 9.5% and orthostatic hypotension 9.4%. 37% had unexplained syncope however most investigators agree that that minimum 40% of these patients may have reflex (Vasovagal syncope).[6,7]

Cheng et al. reported a lifetime cumulative incidence of syncope of 19% in 1925 subjects aged 45 years or older (905 males). 10Recall bias may explain this difference from young.[8-11]

Lipsitz study performed in nursing homes, reported 23% of 711 subjects (54% women) at least one

episode of syncope in past 10 years with 7% episode within previous year.[12] In the two-year follow-up study annual incidence of syncope was 6% compared to 2% incidence reported in the Framingham study. A higher incidence of syncope was found in older patients in nursing homes. This higher incidence may be due to frailer nature of institutional patients and more accurate reporting of the incidence.[13] In the elderly vasovagal syncope is less common but instead cardiac cause of syncope, orthostatic and postprandial hypotension are more common.[14-17] This is due to the diminished efficiency of cardiovascular regulatory system with older age, effects of medications on impairing orthostatic blood pressure control and increased prevalence of organic heart disease(Structural heart disease, cardiac arrhythmia and carotid sinus hypersensitivity).[18,19]

In certain European studies breakdown in different causes of syncope revealed 30 to 40% due to reflex mediated syncope, orthostatic hypotension in 6-24% patients, cardiac syncope in 10-20% patients and psychogenic syncope in 1-5% patients. In 20%patients cause of syncope could not be determined. In emergency department more serious cardiac cause of syncope is common. However reflex mediated syncope remains the most common cause.[20-23]

Alboni etal. performed a study on 341 adult patients (mean age 61 years) for a period of 6 months. After extensive evaluation 23% were diagnosed with cardiac syncope, 54% with reflex syncope and 2% with orthostatic hypotension. Patients with cardiac syncope were much older(72 verses 59 years) and predominantly males (62% vs 47%).[24] Cardiac causes of syncope were more common in elderly (34%) verses young (12%).[25]

A study was conducted by Chen and colleagues on selected patients referred to cardiology clinic. Among 1180 consecutive patients with syncope 571 patients were less than 65 years and 619 patients were older or equal to 65 years. As it was a specifically referred population in those less than 65 years age Vaso-vagal cause accounted for 48.7%, Cardiogenic cause for 20.8%, Orthostatic cause 6%, Carotid sinus hypersensitivity 3.3% and cause was unknown in 19.4%. In those aged 65 years and above Vaso-vagal accounted for 31.2%, Cardiogenic cause 42.1%, Carotid sinus hypersensitivity 9.5%, Orthostatic 3.4% and undetermined cause in 13.6%.[26]

Paling et al performed a study on 101 patients with unexplained fall and 179 patients with unexplained syncope. They used a slightly modified tilt table test/ carotid sinus massage protocol. First carotid sinus massage was done in supine position. If syncope/presyncope was induced the investigations were stopped here. If no syncope or presyncope, subjects were kept at 700 for 15 minutes at the tilt table. If there was no response then Carotid sinus massage was performed during the tilt testing. If no response to Carotid sinus massage, then again sublingual spray of glyceryl trinitrate was administered and the subject kept in the tilt table for 20 min for any response. So, all patients were not subjected to tilt testing and Carotid sinus massage. A positive response in 67/111 patients (60%) with unexplained falls and in 113/179 (63%) with unexplained syncope a difference not statistically significant. The results indicate that many patients with unexplained syncope may have atypical vaso-vagal syncope or carotid sinus syndrome.[27]

Rafanelli et al performed head up tilt table test and Carotid sinus massage by means of the "method of symptoms" on 239 patients with unexplained falls and 989 patients with unexplained syncope. The prevalence of positive tilt table testing was (36%) in patients with unexplained falls and it was lower than those with unexplained syncope (51%). Carotid sinus syncope showed similar prevalence (14% vs 10%). Tilt table testing and Carotid sinus massage had higher positivity rate in group of patients with unexplained falls (61%) and it was similar to the unexplained syncope group (64%). This result suggests that apart from orthostatic hypotension which is common but atypical vasovagal syncope and carotid sinus hypersensitivity may be one of the causes of unexplained falls in elderly.[28]

A Review article Lalit K. Tyagi et al -Showed the major causes of syncope are reflex syncope (60-65% of cases), psychogenic syncope (15-20% of cases), cardiac syncope (15-20% of cases), vascular syncope (2-3% of cases) and metabolic syncope (2-3% of cases). Syncope is a common medical problem and the prevalence of syncope increases with age from 0.7% in men aged 35-44 to 5.6% in men over the age of 75.[29]

Aims and Objectives

1. To find out the prevalence of reflex mediated syncope in a tertiary care hospital.
2. To show that increased cases of Carotid sinus syndrome are detected if carotid sinus massage is done after Head-up tilt table test compared to, if it is done only before.

MATERIALS AND METHODS

Study Duration: April 2020 to June 2021

Study Area- Cardiology outpatient department and indoor at, Apollo Mult speciality Hospitals Limited, Kolkata, a tertiary care hospital.

Study Population- All consecutive adult patients (Age greater than equal to 18 years) who present to cardiology OPD or indoor at, Apollo Mult speciality Hospitals Limited, Kolkata with history of syncope who give consent for the study. Total 150 cases would be taken. Data collection would be stopped once 150 patients are reached. In Apollo multispecialty Hospitals Limited electronic data recording is maintained and International Classification of Diseases coding is followed.

Inclusion Criteria

All adult patients(Age greater than equal to 18 years) who present to cardiology OPD or indoor at, Apollo Multispeciality Hospitals Limited, Kolkata in the time period April 2020 to June 2021 with history of

syncope and in whom Carotid Sinus massage and head-up tilt table test has been ordered as a part of their routine evaluation and who does not meet the exclusion criteria given below. Those patients who gives consent for the study would be included.

Exclusion Criteria-

- Recent history of Myocardial Infarction (within 3 months)
- Transient ischemic attack
- Cerebrovascular accidents
- Ventricular fibrillation or tachycardia
- Carotid bruits
- Seizure disorder
- Valvular heart disease (Aortic stenosis, Mitral stenosis)

Study Tools: A predesigned and pre tested proforma, relevant records and reports, continuous blood pressure recorder, ECG recorder, head-up tilt table, Glyceryl trinitrate spray.

The proforma was prepared in consultation with my guide and co-guide.

Study Technique: Face to face interview to obtain informed consent from the prospective group of patients. Then obtain data on age, sex, comorbid condition, results of blood pressure, carotid sinus massage and head-up tilt table test.

Study Variables: Age, sex, comorbid condition like diabetes mellitus, hypertension, hypothyroidism, blood pressure, head-up tilt table results, carotid sinus massage results

Study Design: This is a cross-sectional, prospective, single centre, observational study. Study is done from February 2020 to June 2021, total 18 months duration. However, 150 sample size is reached then no further subjects are recruited for the study.

Sample Size with Calculation: Alboni etal. performed a study where prevalence of syncope was 54%.38. Formula for sample size calculation in prevalence study is

N= Z2P(1-P)/ d2

Where N= Sample size

Z= Is the statistic corresponding to the level of confidence (for confidence level of 95%,

(Z=1.96)

P= expected prevalence

d= Margin of error.

Sample Size Justification

From the above equation if we take confidence interval of 95%, margin of error as 10% and prevalence of reflex mediated syncope as 54% then the sample size comes as 96. I have taken 150 sample for my study.

Power of Study: After analysing the statistical data (t-test, correlation: Point biserial model) the power of the study was found to be 0.896 (8

Method

It is a prospective observational study with cross-sectional design in a single tertiary care centre with total of 150 patients. All consecutive patients were selected from outdoor and indoor with syncope who presented to Apollo Multispeciality Hospitals Limited, Kolkata. Face to face interview to obtain informed consent from the prospective group of patients. Then obtain data on age, sex, co morbid condition, results of blood pressure, carotid sinus massage and head-up tilt table test were recorded for further analysis.

RESULTS

Statistical analysis was performed with the help of Epi Info (TM) 3.5.3 which is a trademark of the Centers for disease control prevention (CDC).

Age Distribution Statistics

Table 1: Age distribution of study population

Age group	Frequency	Percent	p value	Significance
20-30	3	2.0	< 0.0001	Significant
31-40	7	4.7		
41-50	11	7.3		
51-60	34	22.7		
61-70	66	44.0		
71-80	29	19.3		
Total	150	100.0		

This table is showing the frequency and percentage of age distribution of the study population.

Co-Morbid Condition

Table 2: Table showing co-morbid condition distribution

Co-morbid condition	Frequency	Percent	p value	Significance
HTN	32	21.3	< 0.0001	Significant
T2DM	15	10.0		
T2DM, HTN	40	26.7		
T2DM, Hypothyroid	1	.7		
T2DM, HTN, Hypothyroid	10	6.7		
Nil	52	34.7		
Total	150	100.0		

This table is showing the frequency and the percentage wise distribution of the comorbid condition of the study population.

Table 3: Table showing carotid sinus massage responsedistribution

Carotid sinus massage response	Frequency	Percent	p value	Significance
CIT	13	9.2	< 0.0001	Significant
MT	1	0.7		
Negative	128	90.1		
Total	142	100.0		

Table 4

Head up tilt table test response	Frequency	Percent	p value	Significance
TYPE I	7	6.2	< 0.0001	Significant
TYPE 2A	5	4.4		
TYPE 2B	6	5.3		
TYPE 3	45	39.8		
Negative	50	44.2		
Total	113	100.0		

Total of 113 patient underwent head up tilt test of which Type 3 was the most common positive response

Table 5: (Only positive response in Head up tilt table test)

Head UP tilt qtable test response	Frequency	Percent
TYPE I	7	11.1
TYPE 2A	5	7.9
TYPE 2B	6	9.5
TYPE 3	45	71.5
Total	63	100.0

This table is showing the frequency and percentage wise distribution of various types of positive response in head up tilt table test. 45(71.5%) patients showed type 3 response. 7(11.1%) patients showed type 1 response. 5(7.9%) patients showed type 2A and 6(9.5%) patients showed type 2B response.

Table 6: Disitribution of cause of syncope age <65 years

Cause of syncope(Age<65 years)	frequency
NEUROCARDIOGENIC	43
CARDIOGENIC	11
ORTHOSTATIC	5
CAROTID SINUS SYNDROME	6
UNKNOWN	15
TOTAL	80

DISCUSSION

The above study was done to find out the prevalence of reflex mediated syncope in a tertiary care hospital with a sample size of 150, to find out if chance of detecting Carotid sinus syndrome is increased if carotid sinus massage is done after Head-up tilt table test compared to, if it is done only before. After analyzing the study, the age range was between 20 to 80 years age with mean age 61.2 ±11.5 years (mean±standard deviation) and median of 63 years. Most of the patients are were with age greater than 60 years.

Proportion of male to female was 56.7%:43.3% which was statistically not significant (p=0.102).

Prevalence of neuro-cardiogenic cause of syncope was 42% (63 cases), carotid sinus syndrome was 9.3% (14 cases), cardiogenic cause28% (42 cases), orthostatic hypotension was 4.7% (7 cases) and unknown cause of syncope 16% (24 cases).

Reflex syncope which includes neuro cardiogenic syncope, orthostatic hypotension and carotid sinus syncope accounted for 56% (84 cases).

A similar study was conducted by Chen and colleagues. They found that in 1180 consecutive patients with syncope 571 patients were less than 65 years and 619 patients were older or equal to 65 years. In patients less than 65 years age neuro-cardiogenic cause accounted for 48.7%, Cardiogenic cause for 20.8%, Orthostatic cause 6%, Carotid sinus hypersensitivity 3.3% and cause was unknown in 19.4%. In those aged 65 years and above neuro-cardiogenic accounted for 31.2%, Cardiogenic cause 42.1%, Carotid sinus hypersensitivity 9.5%, Orthostatic 3.4% and undetermined cause in 13.6%.[39]

Alboni etal. performed a study on 341 adult patients (mean age 61 years). The study after extensive evaluation revealed that 23% of the patients were diagnosed with cardiac syncope, 54% with reflex syncope and 2% with orthostatic hypotension. Cardiac causes of syncope were more common in elderly (34%) verses young (12%).[25]

The above-mentioned studies (by Chen etal and Alboni etal) was done in European population and the present study was done in Indian population.

However, when compared to previous studies this study showed similar results.

Neuro-cardiogenic sub type showed Type 1response in11.1%, Type 2A in 7.9%, Type 2B in 9.5% and Type 3 71.5%.

Another study by Gonzalo Baron-Esquivias et al63showed type 1 response in 34.5 %, type 2 response in 27.4 %and type 3 response in non-hypertensive patients while in hypertensive patients it was 31.7%,9.5% and 49.2 % respectively.

The results of the present study were not in accordance with the study done by Gonzalo Baron-Esquivias et al.[30]

Carotid sinus syndrome was diagnosed in 14 patients out of 150. While 12 patients were diagnosed before head up tilt test and 2 further patients were diagnosed when carotid sinus massage was done after head up tilt test. In the study conducted by Abuzeid Eltrafim,[31] and colleagues carotid sinus massage was done in 139 patients of whom 29 showed positive response. 18 that is 62% of these total 29 showed positive response when carotid sinus massage was done after the head-up tilt table test. However, in my study only 14.3% cases were diagnosed with carotid sinus syndrome if carotid sinus massage is performed after head up tilt table test. It is much lesser than the above-mentioned study.

Orthostatic hypotension was detected in 4.7% patients (Total 7 patients) in my study. It was slightly less than the study published by Chen and colleagues.[26]

In patients diagnosed with cardiogenic cause of syncope 10 patients had no comorbidities while 9 had only hypertension, 2 had only diabetes, 18 had both diabetes and hypertension.

In patients diagnosed with carotid sinus syndrome 3 patients had no comorbidities, 3 had only hypertension, 1 had only diabetes, 1 had both diabetes and hypothyroidism, 6 had both diabetes and hypertension.

In patients diagnosed with neuro-cardiogenic syncope 32 patients had no comorbidities, 14 had only hypertension, 7 had only diabetes and 7 had both diabetes and hypertension.

In patients diagnosed with Orthostatic hypotension I patient had no comorbidities while 4 patients had only hypertension while 2 patients had both diabetes and hypertension.

In patients with undiagnosed cause of syncope 6 patients had no comorbidities while 2 had only hypertension, 5 had only diabetes, 7 had both diabetes and hypertension and 4 patients had diabetes, hypertension and hypothyroidism.

In patients less than 65 years age neurocardiogenic cause accounted for54%, Carotid sinus syndrome accounted for 7%, Orthostatic hypotension for 6%, cardiogenic cause accounted for 14% and unknown was 19%.

In patients with age≥ 65 years age neurocardiogenic syncope accounted for 29%, Carotid sinus syndrome 17%, Orthostatic hypotension accounted for 3%, Cardiogenic cause accounted for 44% and unknown in 11%.

In age less than 65 years neurocardiogenic syncope accounted for 54%, Cardiogenic cause accounted for 14%, Orthostatic hypotension accounted for 6%, Carotid sinus syndrome 7% and unknown cause accounted for 19% of the cases. It is almost similar to the study by Chen and colleagues.[26]

In age greater than equal to 65 years neurocardiogenic syncope accounted for 29%, Cardiogenic cause accounted for 44%, Orthostatic hypotension accounted for 3%, Carotid sinus syndrome 13% and unknown cause accounted for 11% of the cases. It is slightly different to the study by Chen and colleagues.[26]

Limitations of the Study

The study was conducted in a single center so the number of patients are lesser compared to large scale observational studies and results of the study may not be generalized to large real-life population.

Study was conducted in a tertiary care center so there was referral bias and hence the study results may not be applicable to the general population.

CONCLUSION

It is better to preform Carotid Sinus Massage both before and after Head up tilt table test as more cases were identified in the study. Reflex syncope remains the most common cause of syncope even in elderly people. Despite detailed evaluation 20% causes of syncope could not be determined.

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