A prospective study on the prevalence of neurally mediated hypotension in systemic lupus erythematosus

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease which affects skin and organ systems. Cardiovascular manifestations are one of the important causes for mortality and morbidity in SLE. Neurally mediated hypotension (NMH) caused by autonomic neuropathy is found to be associated with fibromyalgia responsible for chronic fatigue syndrome in SLE. Our study aims to find the prevalence of NMH in SLE.

Methods: This is a prospective study conducted in the Department of Dermatology, Chengalpattu Medical College from May 2017 to December 2018. All SLE patients who attended the Dermatology OPD were included in the study. The diagnosis of SLE was made based on the ARA criteria. After obtaining informed consent, baseline blood pressure of all patients included in the study were recorded. In patients with low blood pressure other causes of hypotension were ruled out. Patients with no discernible cause of hypotension were subjected to the two stage tilt table test. A drop in systolic BP of >20 mm of Hg or diastolic BP of >10 mm of Hg is considered to be positive.

Results: A total of 20 patients were included in the study, of which 19 were female and one male. The mean age was 31.7 years. 70% of the SLE patients included in our study were found to have NMH.

Conclusions: Neurally Mediated Hypotension was found to be highly prevalent in SLE.

Keywords: Hypotension in SLE, Autonomic neuropathy, Fibromyalgia in SLE, Postural orthostatic tachycardia syndrome

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with a wide range of clinical presentations, associated with multisystem organ inflammation resulting from abnormal immune function due to auto-antibodies that are derived from polyclonal B cell activation and specific antigenic drive. The cardiovascular manifestations of SLE includes pericarditis, myocarditis, libman sacks endocarditis, myocardial infarction, coronary artery disease, pulmonary hypertension, cerebrovascular disease and vasculitis. Neurally mediated hypotension (NMH) has been found in high prevalence in SLE.

NMH is an autonomic dysfunction, where there is an abnormal reflex interaction between the heart and brain, without any structural abnormality. Although NMH-FM is a most common presentation in SLE, NMH can also occur without fibromyalgia. NMH occurrence with SLE is quite common, yet unnoticed. This study aims to find the prevalence of NMH in SLE.
THE METHODS

This is a prospective study conducted in the Department of Dermatology, Chengalpattu Medical College from May 2017 to December 2018. All SLE patients who attended the Dermatology OPD were included in the study. The diagnosis of SLE was made based on the ARA criteria. Patients with known cardiovascular disease, hypotension, or hyperventilation, on anti-hypertensive medications, pregnancy were excluded from the study. After obtaining informed consent, baseline blood pressure of all patients included in the study were recorded. In patients with low blood pressure other causes of hypotension like septic shock, internal hemorrhage or cardiovascular pathology were ruled out. Appropriate investigations like blood culture, USG / CT abdomen was done to rule out occult focal sepsis and internal haemorrhage. ECHO was done to find the left ventricular ejection fraction and collapse of inferior vena cava. Patients with no discernible cause of hypotension were subjected to the two-stage tilt table test.

A provocative tilt test is performed in the morning after the overnight fast or several hours after a meal. In the first phase the patient remains supine for a period of about 15-30 min. ECG and blood pressure recordings are obtained prior to the test and during 30-45 min of tilting. The tilt angle of 60 degrees is optimal. A drop in systolic BP of >20 mm of Hg or diastolic BP of >10 mm of Hg is considered to be positive. Appropriate statistical and inferential analysis was done.

RESULTS

A total of 20 patients were included in the study, of which 19 were female and one male. The mean age was 31.7 years. Three patients had lupus nephritis, two had CNS lupus and one had manifestations of both (Figure 1). The average blood pressure was found to be 97/66 mm of Hg. Fourteen patients had BP less than 100/70 mm of Hg. One patient had hypertension secondary to lupus nephritis. Five patients had normal BP. Out of the 14 patients, 12 were found to have tilt table positive results (Figure 2). 70% of the SLE patients were found to have NMH in our study.

DISCUSSION

In our study we found that about 70% of the SLE patients had NMH, this is in accordance with the study done by Tang et al where they found a prevalence of 47.9% with NMH among 76 patients with SLE.3

NMH is defined as a fall in systolic BP of 20 mm Hg during standing or upright tilt table testing when compared to the BP measured when the person is supine. NMH is more common in persons with a low resting blood pressure. But NMH may also be seen in persons with normal resting blood pressure. NMH is an abnormality in the regulation of blood pressure during upright posture. It occurs due to an abnormal reflex interaction between the heart and the brain, when too little blood circulates back to the heart when people are upright, that results in a lowering of blood pressure. NMH is also known as the fainting reflex, delayed orthostatic hypotension, neurocardiogenic syncope, vasodepressor syncope, vaso-vagal syncope.

NMH should be differentiated from Postural Orthostatic Tachycardia Syndrome and orthostatic hypotension. POTS refers to an exaggerated increase in heart rate with standing. A healthy individual usually has a slight increase in heart rate—by about 10-15 beats per minute—within the first 10 minutes of standing. POTS is considered present if the heart rate increases by 30 beats per minute for adults, or 40 bpm for adolescents, or if it reaches 120 beats per minute or higher over the first 10 minutes of standing, accompanied by orthostatic symptoms.

POTS is an abnormality in the regulation of heart rate; the heart itself is usually normal. Some patients with POTS in the first 10 minutes of upright standing or tilt testing will go on to develop NMH if the test is continued; the two conditions often are found together, and they are not mutually exclusive diagnoses. Both are capable of causing chronic, daily, orthostatic symptoms.

Orthostatic hypotension is not always due to autonomic or other compensatory dysfunction and can be due to
inadequate responses of compensatory mechanisms to environmental stressors. Non-neurogenic OH can be caused by drugs, dehydration, blood loss, age, and illnesses that secondarily cause acute or chronic hypovolemia. For example, dehydration resulting in orthostatic hypotension is not due to autonomic dysfunction and therefore neurogenic orthostatic hypotension is not present; instead, the autonomic and other regulatory systems cannot adequately compensate for the loss of circulating blood volume.

Neurogenic orthostatic hypotension is identified with autonomic failure due to inadequate release of nor-epinephrine from sympathetic vasomotor neurons leading to vasoconstrictor failure.\(^5\) Neurogenic orthostatic hypotension is rare in the young since most causes of autonomic failure are acquired with age either as a primary (e.g., pure autonomic failure) or secondary (diabetes) disease. Autonomic failure can be primary with pre-ganglionic, post-ganglionic, or both (e.g., Parkinson’s disease) forms of sympathetic dysfunction. However, there exist congenital genetic variants such as familial dysautonomia (Riley-Day syndrome) and the exquisitely rare Dopamine Beta-Hydroxylase deficiency (DBH deficiency).\(^6\) Autonomic failure can be autoimmune and may present with SLE, post-infectious Guillain-Barre syndrome although autonomic dysfunction seems to have little effect on ultimate outcome.\(^7,8\)

Autonomic failure is most commonly acquired as a secondary aspect of systemic disease such as diabetes. Sympathetic cardiac denervation is a central aspect of Parkinson’s disease, and may be found in other forms of autonomic failure. Cardiac parasympathetic innervation is also often defective resulting in a steady fall in BP with little reflex tachycardia during orthostatic challenge as shown in the image below.

On the other hand, NMH, in which adrenergic vasoconstriction is defective, is associated with primary autonomic failure; patients with related diseases cannot remain standing and have detectable autonomic abnormalities in all postural positions. It includes any condition with blood flow, heart rate, and cardio-respiratory regulation inadequacy that are demonstrable in the upright position but may also have abnormal findings in all positions. Under such circumstances, it is often the most obvious manifestation of a more widespread impairment in integrative neurovascular physiology. In any patient of SLE, who records a blood pressure less than that of 120/80 mm of Hg, the following algorithm will be exercised to ascertain the cause of hypotension if any such exists in the particular patient in question and if not patient will be ascertained to have NMH after the clinical confirmation by two stage tilt table test.

In patients of SLE recording of BP should be done on three various occasions after annulling anxiety. If patient was found to be anxious, counselling was given and blood pressure was recorded again after 6 hours.

If the patient is found to be normotensive, then the patient is kept under observation and periodic monitoring of BP is done. If found to be hypertensive, then we have to look for pedal edema and do the following investigations to rule out lupus nephritis - Urine routine, 24 hours urine protein, Urine spot PCR, USG abdomen (specific note on outline of kidneys), dsDNA titre if not done previously, C3, C4 levels, Doppler to find out renal artery stenosis and Renal biopsy.

If the patient is found to be hypotensive, then we have to rule out foci of occult sepsis (blood culture, urine culture), Internal haemorrhage, Libmann sacks endocarditis (ECG, ECHO). If the above conditions are ruled out, then perform Two stage tilt table test to confirm NMH.

NMH may or may not be associated with fibromyalgia in SLE patients. NMH per se has no impact on quality of life.\(^9\) The cause for increased incidence of NMH in SLE is yet to be determined. Identification of NMH is important in SLE patients who have chronic fatigue. NMH cannot explain the increased prevalence of FM in SLE.\(^4\)

**CONCLUSION**

NMH is common in SLE patients. NMH-FM in patients of SLE is responsible for the chronic fatigue syndrome and the unexplained malaise which is the hallmark of SLE patients. The treating physician must be aware of the above fact, so that we need not panic about SLE patients with persistent hypotension, which stabilizes as the disease activity comes down.

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**REFERENCES**


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