Diabetes May Accelerate the Onset of Orthostasis

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INTRODUCTION

Orthostasis can be a debilitating disorder of the autonomic nervous system, with the associated vertigo effecting quality of life and daily activities [Freeman, 2003]. Many diabetics report vertigo as one of a list of symptoms with which they must contend. Vertigo can be a result of orthostatic abnormalities, including drops in blood pressure and excessive increases in heart rate upon assuming an upright posture (stand) [Borst, *et al.*, 1982; Smit, *et al.*, 1999]. Clinical orthostasis is predicated on very specific levels of change in either BP or HR [Boulton, *et al.*, 2005; Maser and Lenhard, 2005].

Sympathetic Withdrawal (SW) is a physiologic definition of orthostasis. Empirical evidence suggests that SW is associated with vertigo and occurs prior to the abnormal changes in BP or HR associated with orthostasis. Further empirical and clinical evidence suggests correcting SW, even prior to the onset of clinical orthostasis, can relieve the complaints of vertigo and this can be accomplished with low dose, shorter term therapy. Therefore, SW can be an early marker of the onset of orthostasis.

We studied the effect of diabetes on the onset of orthostasis. Physiologically, orthostasis can be defined as a decrease in sympathetic activity in response to a postural change (SW). Normally, sympathetic activity should increase upon assuming an upright posture. But, the amount of increase decreases with age. We hypothesized that the decrease in sympathetic change while assuming an upright posture happens at earlier ages in people with diabetes.

METHOD

ANS function testing (ANX3.0, ANSAR Inc. Philadelphia, PA) was performed on 63 normal subjects (age: 41 ± 12; 34 Female) and 43 diabetic patients (age: 46 ± 11; 20 Female, 35 NIDDM). ANS function testing was based on spectral analysis of both respiratory and heart rate variability signals [Vinik, *et al.*, 2004]. The resulting low frequency area (LFa) is a measure of sympathetic activity, and with this methodology is a better measure of sympathetic change in orthostasis than the LFa/RFa ratio [Stoupakis, *et al.*, 2002]. Stand LFa (SLfa) and Baseline LFa (BxLfa) are calculated from a five minute upright postural period (S) that follows a five minute resting period (Bx). The average difference between SLFa and BxLFa (SLfa-BxLfa) are plotted against age for normal subjects and diabetic patients. Differences between diabetics and normals are evaluated by nonparametric statistical tests.

RESULTS

There was a significant negative correlation between (SLfa-BxLfa) and age in normal subjects ($r = -0.37$; $p < 0.01$). A negative correlation was also observed for diabetic patients but it was not significant. SLFa-BxLFa was significantly lower in diabetes (0.10 ± 1.05) than in normal subjects (1.66 ± 3.87) ($p < 0.05$). Sympathetic increase in normals' response to stand was always lower in each successive age group (Fig. 1). In diabetic patients, the sympathetic increase upon standing is lower for each age group as compared to normals and turns negative (becomes SW) in patients of more than 50 years (Fig. 1). SLFa-BxLFa was never negative in the normal subjects. Change in Diastolic BP from Bx to S was significantly lower in diabetic subjects (0.30

± 7.22 mmHg) than in normal subjects (4.85 ± 6.98 mmHg) ($p < 0.01$). Change in systolic BP and mean HR from Bx to S was not significantly different between the two populations.

CONCLUSION

The sympathetic surge expected upon standing is significantly diminished in diabetes as compared to normals. Sympathetic surge becomes SW in diabetics around age 50, on average. This is reflected in a smaller change in BP upon standing in these patient. SW may foreshadow the onset of Orthostasis.

REFERENCES

Borst C,Weiling W, van Brederode JFM, et al. Mechanisms of initial heart rate response to postural change. Am J Physiol. 1982; 243: H676–H681.

Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, Malik RA, Maser RE, Sosenko JM, Ziegler D; American Diabetes Association. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005 Apr;28(4):956-62.

Freeman R. Treatment of orthostatic hypotension. Seminars in Neurol. 2003; 23(4), 435-42.

Maser RE, and Lenhard MJ. Cardiovascular autonomic neuropathy due to diabetes mellitus: clinical manifestations, consequences, and treatment. J Clin Endocrinol Metab, 2005. 90(10): p. 5896-903.

Smit AA, Halliwill JR, Low PA, Wieling W. Pathophysiological basis of orthostatic hypotension in autonomic failure. J Physiol 1999;519(Pt 1):1–10.

Stoupakis G, Colombo J, Rendas-Baum R, Budhwani N, Arora R. (2002) Postural drop of low frequency component of heart rate variability in the diagnosis of orthostasis. AHA Abstr., Chicago, IL.

Vinik AI, Aysin B, Colombo J. Enhanced frequency domain analysis replaces older heart rate variability methods. Fourth Annual Diabetes Technology Meeting 28-30 October, 2004.

Table 1: Differences between Normal and Diabetic Subjects (**: p<0.01; NS: Not significant)

		Normal (n=63)	**Diabetic (n=43)**	**p**
Baseline	Mean HR	74.8±12.8	76.1±12.9	NS
	Range HR	21±6	15±6	0.000**
	Systolic BP	120±14	129±17	0.005**
	Diastolic BP	72±11	75±10	NS
Stand	Mean HR	83.6±13.9	84.4±13.8	NS
	Range HR	29±13	23±8	0.001**
	Systolic BP	122±17	133±21	0.007**
	Diastolic BP	77±11	75±9.0	NS

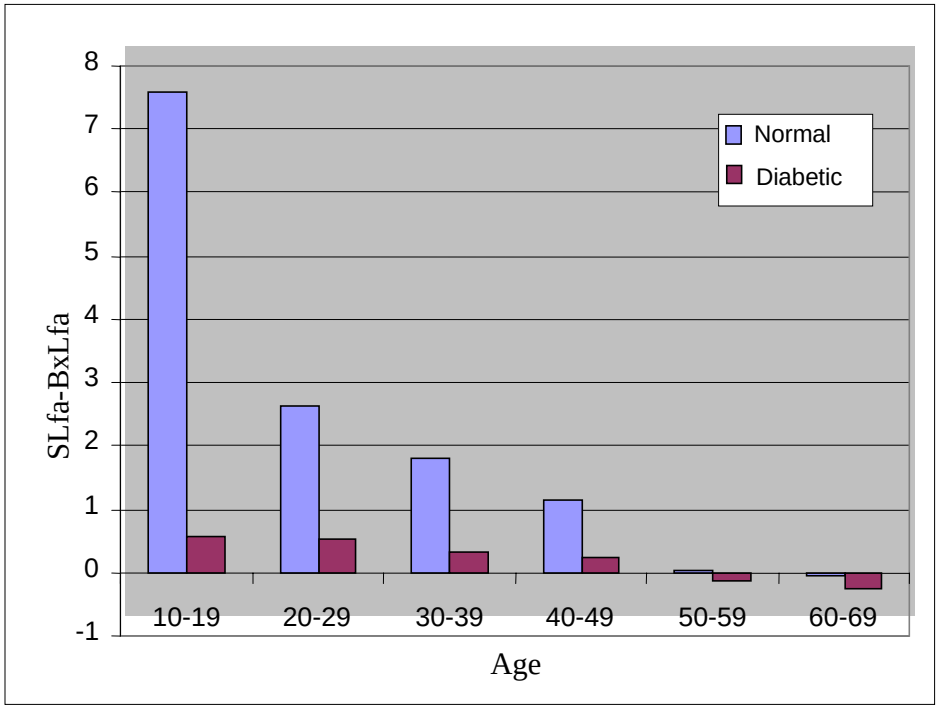

Figure 1: Change in sympathetic tone from baseline to stand (SLfa-BxLfa) vs. age in normal and diabetic subjects. SLfa-BxLfa was negatively correlated with age in normal and diabetics. Correlation was significant in normal subjects ($p < 0.01$). In Diabetes patients, SLfa-BxLfa was always lower and it became abnormally negative around 50 years of age.