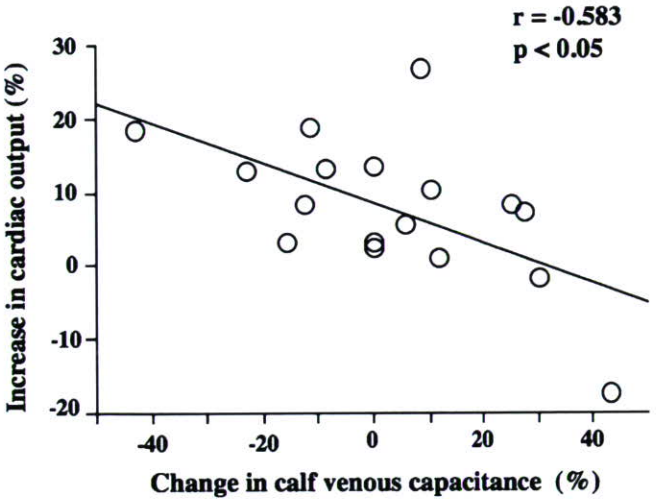

Fig. 6 Change in calf venous capacitance showed significant negative correlation with increase in cardiac output after glucose ingestion across the whole MSA population ($r = -0.583$, $p < 0.05$)

Frequency of OH was slightly higher in MSA with PPH than in MSA without PPH, but the difference was not significant. NE supersensitivity was demonstrated more frequently in MSA with PPH than in MSA without PPH, but the difference was not significant. Plasma NE was slightly lower in MSA with PPH than in MSA without PPH or in controls, but the difference was not significant. Plasma NE levels were not significantly correlated with HR and with CVC changes after glucose ingestion across the whole MSA population. Plasma AVP in MSA with PPH was slightly but not significantly higher than in MSA without PPH or in controls (Table 1).

Discussion

Reduced CVC and increased cardiac output after glucose ingestion were demonstrated in MSA without PPH and in controls, while in contrast CVC increased after ingestion in MSA with PPH. The change in CVC showed a negative correlation with the increase in cardiac output. Furthermore, the change in CVC after glucose ingestion correlated positively with the decrease in SBP and DBP. The venous system has been found to normally contain 64% of total blood volume while showing great distensibility, as to represent a reserve compartment for circulating blood volume [22]. Regulation of venous capacitance thus plays an important role in homeostasis of the systemic circulation system. A reduction of venous capacitance increases effective intravascular volume that results in an increase in cardiac output. A physiologic decline in venous capacitance can contribute importantly to systemic compensation for increased splanchnic blood flow induced by a meal; failure of venous capacitance reduction to occur is one of the factors underlying PPH, especially in MSA.

The precise mechanism of PPH has not been fully clarified. As presently understood, the causative sequence would begin with food ingestion inducing an increase in splanchnic blood flow [19, 24], and release of vasodilatory gastrointestinal peptides such as neurotensin [1, 8, 16]; as a result, systemic blood pressure tends to decrease. In normal subjects, the sympathetic nervous system is then activated to prevent systemic hypotension. However, this compensatory system is compromised in patients with autonomic failure, this defect eventually can result in PPH. Previous studies have shown evidence of impaired sympathetic compensation in PPH patients, including diminished baroreflex function, blunted compensatory increases in cardiac output, impairment of physiologic increases in muscle sympathetic nerve activity [6], and insufficient peripheral vasoconstriction [10, 13, 16]. These response defects are compatible with our previous finding that simultaneous treatment with β_1 and α_1 agonists sufficiently increased cardiac output and vascular resistance to prevent PPH [11]. The present study implicates defective regulation of venous capacitance as an important contributor to PPH. A notable finding in this study is that CVC after glucose ingestion not only failed to decrease, but actually increased in MSA with PPH. The mechanism resulting in elevation is not clear, and further studies are necessary.

In this study HR did not change in MSA patients, even when SBP decreased significantly. This compromised physiologic response suggests that impaired baroreflex function also contributes to PPH in MSA. Thus, PPH appears to result from an interplay of several mechanisms.

MSA with PPH showed somewhat more frequent NE supersensitivity than MSA without PPH, while falling short of significance. NE denervation supersensitivity suggests that postganglionic sympathetic neurons are affected in this MSA subgroup. Thus, MSA with PPH had more severely impaired autonomic function than MSA without PPH. As the illness progresses, MSA patients have increasing difficulty maintaining an upright posture, so PPH becomes a more troublesome symptom than OH. The frequency of clinical PPH was low even in the group diagnosed as PPH by glucose loading test. PPH is a symptom that patients often fail to notice, although it can lead to severe clinical problems such as cardiac and cerebral ischemia [13, 26]. Not only patients but also caregivers and health care staffs need to keep alert to possible consequences of PPH.

References

1. Carraway R, Leeman SE (1973) The isolation of a new hypotensive peptide, neurotensin, from bovine hypothalami. J Biol Chem 248:6854–6861
2. Forconi S, Jageneau A, Guerrini M, Pecchi S, Cappelli R (1979) Strain gauge plethysmography in the study of circulation of the limbs. Angiology 30:487–497
3. Fu Q, Iwase S, Niimi Y, Kamiya A, Michikami D, Mano T, Suzumura A (2002) Age-related influences of leg vein filling and emptying on blood volume redistribution and sympathetic reflex during lower body negative pressure in humans. Jpn J Physiol 52:77–84
4. Gilman S, Low PA, Quinn N, Albanese A, Ben-Shlomo Y, Fowler CJ, Kaufmann H, Klockgether T, Lang AE, Lantos PL, Litvan I, Mathias CJ, Oliver E, Robertson D, Schatz I, Wenning GK (1999) Consensus statement on the diagnosis of multiple system atrophy. J Neurol Sci 163:94–98
5. Gladstone SA (1935) Cardiac output and related functions under basal and postprandial conditions. Arch Intern Med 55:533–546
6. Hakusui S, Sugiyama Y, Iwase S, Hasegawa Y, Koike Y, Mano T, Takahashi A (1991) Postprandial hypotension: microneurographic analysis and treatment with vasopressin. Neurology 41:712–715
7. Halliwill JR, Minson CT, Joyner MJ (1999) Measurement of limb venous compliance in humans: technical considerations and physiological findings. J Appl Physiol 87:1555–1563
8. Hirayama M, Ieda T, Koike Y, Takeuchi Y, Takeuchi S, Sakurai N, Hakusui S, Hasegawa Y, Takahashi A (1994) Pathophysiology of postprandial hypotension in patients with progressive autonomic failure (6)—comparison of gut peptide responses to oral intake of glucose and protein. Auton Nerv Syst 31:47–51
9. Hirayama M, Koike Y (1997) Pharmacological test. Nippon Rinsho 55(Suppl 1):491–493
10. Hirayama M, Watanabe H, Koike Y, Hasegawa Y, Kanaoke Y, Sakurai N, Hakusui S, Takahashi A (1993) Postprandial hypotension: hemodynamic differences between multiple system atrophy and peripheral autonomic neuropathy. J Auton Nerv Syst 43:1–6
11. Hirayama M, Watanabe H, Koike Y, Kanaoke Y, Sakurai N, Hakusui Y, Takahashi A (1993) Treatment of postprandial hypotension with selective alpha 1 and beta 1 adrenergic agonists. J Auton Nerv Syst 45:149–154
12. Hokanson DE, Sumner DS, Strandness DE Jr (1975) An electrically calibrated plethysmograph for direct measurement of limb blood flow. IEEE Trans Biomed Eng 22:25–29
13. Jansen RW, Lipsitz LA (1995) Postprandial hypotension: epidemiology, pathophysiology, and clinical management. Ann Intern Med 122:286–295
14. Lipsitz LA, Fullerton KJ (1986) Postprandial blood pressure reduction in healthy elderly. J Am Geriatr Soc 34:267–270
15. Mathias CJ, Bannister R (1999) Investigation of autonomic disorders. In: Bannister R, Mathias CJ (eds) Autonomic failure. A textbook of clinical disorders of the autonomic nervous system, 4th ed. Oxford University Press, pp 171–175
16. Mathias CJ, da Costa DF, Fosbraey P, Bannister R, Wood SM, Bloom SR, Christensen NJ (1989) Cardiovascular, biochemical and hormonal changes during food-induced hypotension in chronic autonomic failure. J Neurol Sci 94:255–269
17. Mathias CJ, Holly E, Armstrong E, Shareef M, Bannister R (1991) The influence of food on postural hypotension in three groups with chronic autonomic failure—clinical and therapeutic implications. J Neurol Neurosurg Psychiatr 54:726–730
18. Micieli G, Martignoni E, Cavallini A, Sandrini G, Nappi G (1987) Postprandial and orthostatic hypotension in Parkinson's disease. Neurology 37:386–393
19. Norryd C, Dencker H, Lunderquist A, Olin T, Tylen U (1975) Superior mesenteric blood flow during digestion in man. Acta Chir Scand 141:197–202
20. Seyer-Hansen K (1977) Postprandial hypotension. Br Med J 2:1262
21. Smirk FM (1953) Action of a new methonium compound (M&B 2050A) in arterial hypertension. Lancet 1:457–464
22. Smith JJ, Kampine JP (1990) Blood and the ciuculation: general features. In: Smith JJ, Kampine JP (eds) Circulatory physiology, 3rd ed. Williams & Wilkins, pp 1–15
23. Stewart JM (2002) Pooling in chronic orthostatic intolerance: arterial vasoconstrictive but not venous compliance defects. Circulation 105:2274–2281
24. Svensson CK, Edwards DJ, Mauriello PM, Barde SH, Foster AC, Lanc RA, Middleton E Jr, Lalka D (1983) Effect of food on hepatic blood flow: implications in the "food effect" phenomenon. Clin Pharmacol Ther 34:316–323
25. Thomaides T, Bleasdale-Barr K, Chaudhuri KR, Pavitt D, Marsden CD, Mathias CJ (1993) Cardiovascular and hormonal responses to liquid food challenge in idiopathic Parkinson's disease, multiple system atrophy, and pure autonomic failure. Neurology 43:900–904
26. Yokota T, Kamata T, Mitani K (1997) Postprandial cerebral ischemia. Stroke 28:2322–2323