



## COMPLICATIONS AND CO MORBID CONDITIONS OF ORTHOSTATIC HYPOTENSION – AN OVERVIEW

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### ABSTRACT

Orthostatic hypotension (OH), defined as a fall in blood pressure when a person moves from a lying to standing position, is a common physical finding in older adults. It is associated with numerous medical conditions. Its prevalence increases with age and treatment is specific to the cause. Drug-induced OH can be alleviated by changing medications or reducing dosage. OH secondary to autonomic insufficiency or neurogenic causes remains a challenge to manage, and a combination of pharmacologic and non-pharmacologic measures are needed. In this review, various complications of OH in conjunction with co morbid conditions are discussed.

**Keywords:** Orthostatic hypotension, Elderly, Complications.

### INTRODUCTION

Orthostatic hypotension is an important risk factor for cardiovascular diseases and all-cause mortality<sup>1-7</sup>. Depending on method used to measure OH, prevalence is between 5 to 30%<sup>3-7</sup>. The American Autonomic Society and the American Academy of Neurology have defined OH as a reduction in systolic blood pressure (SBP) or diastolic blood pressure (DBP) by 20 and 10 mmHg, respectively, within 3 min of standing<sup>8</sup>.

Orthostatic hypotension is a debilitating, chronic illness and is difficult to treat. The therapeutic goals aim to improve postural symptoms, standing time, and function rather than to achieve upright normotensive state, which can lead to supine hypertension. Drug therapy alone is not adequate to treat OH<sup>9</sup>. OH secondary to autonomic insufficiency or neurogenic causes is a big challenge to clinicians and a combination of pharmacologic and non-pharmacologic measures are needed to manage<sup>10</sup>.

All the relevant information on complications of orthostatic hypotension was collected through MEDLINE/PUBMED. The evidence presented in this review has showed that prevention of complications of orthostatic hypotension among older adults is of paramount importance to reduce mortality and morbidity associated with orthostatic hypotension.

### SYNCOPE AND ORTHOSTATIC HYPOTENSION

Endurance athletes who showed OH were not at a higher risk of syncope than those who showed lesser reductions in blood pressure. Post-exercise hypotension, initial OH and residual initial OH could not predict the time to develop syncope after a prolonged exercise<sup>11</sup>. In a retrospective study on patients of syncope, changing pattern in the etiology was observed with increase in age. The disease burden was high in the elderly<sup>12</sup>.

Study done on patients with postural tachycardia syndrome showed syncope (both tilt table and clinical) occurred more commonly in patients with postural tachycardia syndrome than patients who had orthostatic hypotension. The low-pressure baroreceptor system implicated in postural tachycardia syndrome confers more sensitivity to syncope than high pressure system implicated in orthostatic hypotension<sup>13</sup>. Patients with mild dementia with Lewy bodies showed symptom of orthostatic hypotension<sup>14</sup>. Orthostatic symptoms in patients with Parkinson's disease had a high specificity but low sensitivity in predicting orthostatic hypotension<sup>15</sup>. In a 40-year-old man with three syncopal episodes, tilt test induced marked hypotension and bradycardia after nitroglycerine administration. Arrhythmia had role in the etiology of symptoms with respect to autonomic impairment<sup>16</sup>.

The common cardiac disorders linked to syncope and falls were carotid sinus syndrome, postprandial hypotension, vasovagal syncope, orthostatic hypotension and bradyarrhythmias<sup>17</sup>. A rare sub form of orthostatic hypotension with recurrent syncope occurred following bilateral carotid artery surgery and radiation, suggesting baro reflex failure. Treatment with clonidine improved both high blood pressure and orthostatically induced syncope. OH was often associated with many co morbid conditions leading to several complications<sup>18</sup>.

### TRANSIENT ISCHAEMIC ATTACK

Patient with bilateral carotid occlusion developed left motor seizures and bilateral transient ischemic attacks after a reversible right hemispheric stroke, both triggered by OH<sup>19</sup>. In patients with type 1 diabetes cardiovascular autonomic neuropathy was associated with impaired dynamic cerebral auto regulation. The magnitude of dynamic cerebral auto regulation impairment increased



with the severity of cardiovascular autonomic neuropathy<sup>20</sup>. Spontaneous intracranial hypotension presenting with postural or exertional headaches was associated with bilateral abducens palsy<sup>21</sup>. OH was present in 22% of vascular dementia subjects, 15% in Alzheimer's disease subjects, 12% in mild cognitive impairment subjects<sup>22</sup>. Orthostatic hypertension occurred due to impairment of cerebellar autonomic modulation in a 20-year-old man with a cerebellar hematoma and acute hydrocephalus, who had a vermian and partial right cerebellar hemisphere resection<sup>23</sup>. Orthostatic hypotension interfered with usage of standing apparatus in a large proportion of patients with spinal cord injury<sup>24</sup>.

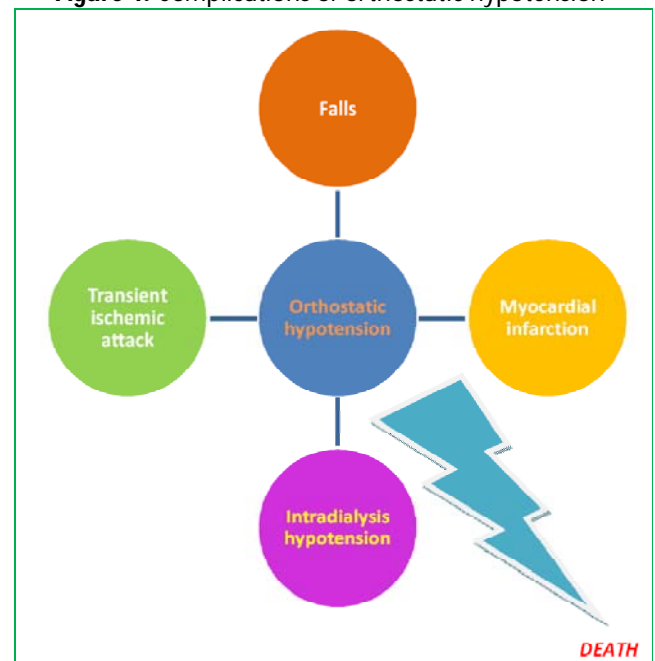
A 78 year old male person experienced repeated transient ischemic attacks, each time after ingestion of food and showed postprandial and orthostatic hypotension<sup>25</sup>. In patients with neurogenic OH, those with cardiac sympathetic denervation had an impaired inotropic response to tyramine and exaggerated response to isoproterenol. Cardiac denervation was associated with decreased ability to release endogenous norepinephrine from sympathetic nerves<sup>26</sup>. Parkinson's disease patients have OH as a common finding. In them, Parkinson's disease with OH should not be mistaken for multiple system atrophy<sup>27</sup>. Frequency and severity of OH were more in cerebellar variant of multiple system atrophy followed by Parkinson variant of multiple system atrophy and idiopathic Parkinson's disease<sup>28</sup>. Frequency of orthostatic hypotension in patients with Parkinson's disease was 40.2%. The longer duration and advanced stage of Parkinson's disease and selegiline usage were the factors associated with this condition<sup>29</sup>.

### MYOCARDIAL INFARCTION

Diastolic blood pressure drop on standing up identified subjects at a high risk of subsequent myocardial infarction in a study on home dwelling elderly population<sup>30</sup>. In an elderly Hispanic man with complaints of dizziness upon standing with no history of heart murmurs or syncope, physical examination revealed evidence of orthostatic hypotension suggesting a correlation between orthostasis and an atrial myxoma<sup>31</sup>. In middle-aged hypertensive subjects, orthostatic hypotension predicted the incidence of atrial fibrillation, independent to conventional risk factors<sup>32</sup>. In a cross-sectional study conducted on hypertensives and normotensives, aged 40-75 years, orthostatic hypotension was associated with cardiovascular risk and target organ damage<sup>33</sup>. Orthostatic hypotension results to reverse dipping. Orthostatic hypotension is a more robust predictor of cardiovascular events than reverse dipping in the elderly<sup>34</sup>. In patients with delayed OH, the progressive decrease of systolic blood pressure was associated with progressive decrease in total peripheral resistance. Cardiac output and stroke volume showed little variation<sup>35</sup>. Orthostatic hypotension increased the risk of coronary heart disease and all cause mortality in elderly people<sup>36</sup>.

Hypertensive patients with greater change of postural blood pressure (OH and orthostatic hypertension) had an increased risk of advanced silent brain lesions and higher cardiac burden<sup>37</sup>. In hypertensive patients, orthostatic hypertension was positively associated with peripheral arterial disease. Orthostatic hypotension was significantly associated with peripheral arterial disease and left ventricular hypertrophy. No association was found between orthostatic hypertension or hypotension and a decreased estimated glomerular filtration rate<sup>33</sup>. Posture-related changes in intra ocular pressure occur in patients with autonomic failure, due to posture-induced changes in systemic blood pressure<sup>38</sup>.

**Figure 1: Complications of orthostatic hypotension**



### DEATH

Increased mortality predicted by blood pressure fall on standing was associated with injuries, neurodegenerative, and respiratory diseases, and cardiovascular disease in elderly people. Both increase as well as decrease of systolic blood pressure during early orthostasis indicate greater risk of cerebrovascular death<sup>39</sup>.

### OH AND KIDNEY DISEASE

OH was an important risk factor for chronic kidney disease in middle-aged persons. The effect of race varied with the definition of chronic kidney disease<sup>40</sup>. Common adverse drug effects associated with antihypertensive usage in older adults with chronic kidney disease were hyperkalemia, acute kidney injury and orthostatic hypotension<sup>41</sup>. Presence of OH in the introductory phase of hemodialysis was a novel independent predictor of all-cause mortality<sup>42</sup>. In patients on hemodialysis, intradialysis hypotension and orthostatic hypotension after hemodialysis were significant and independent factors affecting mortality<sup>43</sup>. OH and hypotension were

associated with target organ damage in middle and old-aged hypertensive patients<sup>44</sup>.

## CONCLUSION

It is very difficult to ascertain the etiology of orthostatic hypotension in elderly patients with several age related changes and multiple medications. Therapeutic intervention for orthostatic patients may vary depending on the associated co morbid condition. Diagnosis or onset of OH should prompt the clinician to consider other conditions, especially if the patient is elderly.

## REFERENCES

- Rose KM, Tyroler HA, Nardo CJ, Arnett DK, Light KC, Rosamond W, Sharrett AR, Szklo M, Orthostatic hypotension and the incidence of coronary heart disease: the Atherosclerosis Risk in Communities study. *Am J Hypertens*, 13:2000, 571-578.
- Eigenbrodt ML, Rose KM, Couper DJ, Arnett DK, Smith R, Jones D, Orthostatic hypotension as a risk factor for stroke: the atherosclerosis risk in communities (ARIC) study, 1987-1996. *Stroke*, 31:2000, 2307-2313.
- Luukinen H, Koski K, Laippala P, Kivela SL, Prognosis of diastolic and systolic orthostatic hypotension in older persons. *Arch Intern Med* 159: 1999, 273–280.
- Rutan GH, Hermanson B, Bild DE, Kittner SJ, LaBaw F, Tell GS, Orthostatic hypotension in older adults, The Cardiovascular Health Study, CHS Collaborative Research Group. *Hypertension*, 19:508-519.
- Ooi WL, Barrett S, Hossain M, Kelley-Gagnon M, Lipsitz LA, Patterns of Orthostatic blood pressure change and their clinical correlates in a frail, elderly population. *JAMA* 277: 1997, 1299–1304.
- Masaki KH, Schatz IJ, Burchfiel CM, Sharp DS, Chiu D, Foley D, Curb JD, Orthostatic hypotension predicts mortality in elderly men: the Honolulu Heart Program. *Circulation* 98: 1998, 2290–2295.
- Davis BR, Langford HG, Blaufox MD, Curb JD, Polk BF, Shulman NB, The association of postural changes in systolic blood pressure and mortality in persons with hypertension: the Hypertension Detection and Follow-up Program experience. *Circulation* 75: 1987, 340–346.
- John G. Bradley MD and Kathy A. Davis RN, Orthostatic Hypotension. *Am Fam Physician*, 68: 2003, 2393-2399.
- Figueroa JJ, Basford JR, Low PA, Preventing and treating orthostatic hypotension: As easy as A, B, C. *Cleve Clin J Med*, 77:2010, 298-306.
- Sclater A, Alagiakrishnan K, Orthostatic hypotension: A primary care primer for assessment and treatment. *Geriatrics*, 59:2004, 22-27.
- Murrell CJ, Cotter JD, George K, Shave R, Wilson L, Thomas K, Williams MJ, Ainslie PN, Syncope is unrelated to supine and postural hypotension following prolonged exercise. *Eur J Appl Physiol*, 111:2011, 469-476.
- Cooke J, Carew S, Costelloe A, Sheehy T, Quinn C, Lyons D, The changing face of orthostatic and neurocardiogenic syncope with age. *QJM, An International Journal of Medicine*, 7, 2011.
- Ojha A, McNeeley K, Heller E, Alsheklee A, Chelimsky G, Chelimsky TC, Orthostatic syndromes differ in syncope frequency. *Am J Med*, 123:2010, 245-249.
- Sonnensyn H, Nilsen DW, Rongve A, Nore S, Ballard C, Tysnes OB, Aarsland D, High prevalence of orthostatic hypotension in mild dementia. *Dement Geriatr Cogn Disord*, 28:2009, 307-313.
- Jamnadas-Khoda J, Koshy S, Mathias CJ, Muthane UB, Ragothaman M, Dodaballapur SK, Are current recommendations to diagnose orthostatic hypotension in Parkinson's disease satisfactory? *Mov Disord*, 24:2009, 1747-1751.
- Reato S, Baratella MC, D'este D, Persistent atrial fibrillation associated with syncope due to orthostatic hypotension: a case report. *J Cardiovasc Med (Hagerstown)*, 10: 2009 Nov, 866-868.
- Cronin H, Kenny RA, Cardiac causes for falls and their treatment. *Clin Geriatr Med*, 26:2010, 539-567.
- Frantz S, Lührs H, Allolio B, Koller ML, Recurrent hypertensive crises associated with severe orthostatic hypotension due to baroreflex failure syndrome. *Z Kardiol*, 91 :2002, 946-950.
- G. Landi, P. Perrone and M. Guidotti, Bilateral TIAs and unilateral seizures due to orthostatic hypotension. A case report. *The Italian Journal of Neurological Sciences*, 4, 239-241.
- Nasr N, Czosnyka M, Arevalo F, Hanaire H, Guidolin B, Larrue V, Autonomic neuropathy is associated with impairment of dynamic cerebral autoregulation in type 1 diabetes. *Auton Neurosci*, 160 :2011, 59-63.
- Porta-Etessam J, Di Capua D, Jorquera M, Cuadrado ML, Marcos A, Orthostatic headache and bilateral abducens palsy secondary to spontaneous intracranial hypotension. *J Headache Pain*, 12 :2011, 109-111.
- Mehrabian S, Duron E, Labouree F, Rollot F, Bune A, Traykov L, Hanon O, Relationship between orthostatic hypotension and cognitive impairment in the elderly. *J Neurol Sci*, 299:2010, 45-8.
- Idiaquez J, Fadic R, Mathias CJ, Transient orthostatic hypertension after partial cerebellar resection. *Clin Auton Res*, 21 : 2011, 57-9.
- Chelvarajah R, Knight SL, Craggs MD, Middleton FR, Orthostatic hypotension following spinal cord injury: impact on the use of standing apparatus. *NeuroRehabilitation*, 24 : 2009, 237-242.
- Kamata T, Yokota T, Furukawa T, Tsukagoshi H, Cerebral ischemic attack caused by postprandial hypotension. *Stroke*, 25:1994, 511-513.
- Imrich R, Eldadah BA, Benthoo O, Pechnik S, Sharabi Y, Holmes C, Grossman E, Goldstein DS, Functional effects of cardiac sympathetic denervation in neurogenic orthostatic hypotension. *Parkinsonism Relat Disord*, 15:2009, 122-7.
- Goldstein DS, Orthostatic hypotension as an early finding in Parkinson's disease. *Clin Auton Res*, 16:2006, 46-54.



28. Wenning GK, Granata R, Krismer F, Dürr S, Seppi K, Poewe W, Bleasdale-Barr K, Mathias CJ, Orthostatic Hypotension Is Differentially Associated with the Cerebellar Versus the Parkinsonian Variant of Multiple System Atrophy: a Comparative Study. *Cerebellum*, 2011, 6.
29. Sithinamsuwan P, Orrawanhanonthai P, Thithum K, Udommongkol C, Chairangsaris P, Chinvarun Y, Nidhinandana S, Wongmek W, Suphakasem S, Suwantamee J, Orthostatic hypotension: a non-motor complication assessment in 82 patients with idiopathic Parkinson's disease in Phramongkutklo Hospital. *J Med Assoc Thai*, 93:2010, S93-99.
30. Luukinen H, Koski K, Laippala P, Airaksinen KE, Orthostatic hypotension and the risk of myocardial infarction in the home-dwelling elderly. *J Intern Med*, 255:2004, 486-493.
31. Vicari RM, Polanco E, Schechtmann N, Santiago JO, Shaurya K, Halstead M, Marszal D, Grosskreutz T, Thareja S, Atrial myxoma presenting with orthostatic hypotension in an 84-year-old Hispanic man: a case report. *J Med Case Reports*, 3:2009, 9328.
32. Fedorowski A, Hedblad B, Engström G, Gustav Smith J, Melander O, Orthostatic hypotension and long-term incidence of atrial fibrillation: the Malmö Preventive Project. *J Intern Med*, 268:2010, 383-389.
33. Fan XH, Wang Y, Sun K, Zhang W, Wang H, Wu H, Zhang H, Zhou X, Hui R, Disorders of orthostatic blood pressure response are associated with cardiovascular disease and target organ damage in hypertensive patients. *Am J Hypertens*, 23:2010, 829-837.
34. Fagard RH, De Cort P, Orthostatic hypotension is a more robust predictor of cardiovascular events than nighttime reverse dipping in elderly. *Hypertension*, 56: 2010, 56-61.
35. Podoleanu C, Maggi R, Oddone D, Solano A, Donateo P, Croci F, Carasca E, Ghingina C, Brignole M, The hemodynamic pattern of the syndrome of delayed orthostatic hypotension. *J Interv Card Electrophysiol*, 26:2009, 143-149.
36. Verwoert GC, Mattace-Raso FU, Hofman A, Heeringa J, Stricker BH, Breteler MM, Witteman JC, Orthostatic hypotension and risk of cardiovascular disease in elderly people: the Rotterdam study. *J Am Geriatr Soc*, 56:2008, 1816-1820.
37. Eguchi K, Kario K, Hoshida S, Hoshida Y, Ishikawa J, Morinari M, Hashimoto T, Shimada K, Greater change of orthostatic blood pressure is related to silent cerebral infarct and cardiac overload in hypertensive subjects. *Hypertens Res*, 27:2004, 235-241.
38. Dumskyj MJ, Mathias CJ, Doré CJ, Bleasdale-Barr K, Kohner EM, Postural variation in intraocular pressure in primary chronic autonomic failure. *J Neurol*, 249:2002, 712-718.
39. Fedorowski A, Hedblad B, Melander O, Early postural blood pressure response and cause-specific mortality among middle-aged adults. *Eur J Epidemiol*, 26:2011, 537-546.
40. Franceschini N, Rose KM, Astor BC, Couper D, Vupputuri S, Orthostatic hypotension and incident chronic kidney disease: the atherosclerosis risk in communities study. *Hypertension*, 56:2010,1054-1059.
41. Marcum ZA, Fried LF, Aging and antihypertensive medication-related complications in the chronic kidney disease patient. *Curr Opin Nephrol Hypertens*, 20:2011, 449-456.
42. Sasaki O, Nakahama H, Nakamura S, Yoshihara F, Inenaga T, Yoshii M, Kohno S, Kawano Y, Orthostatic hypotension at the introductory phase of haemodialysis predicts all-cause mortality. *Nephrol Dial Transplant*, 20:2005, 377-381.
43. Shoji T, Tsubakihara Y, Fujii M, Imai E, Hemodialysis-associated hypotension as an independent risk factor for two-year mortality in hemodialysis patients. *Kidney Int*, 66:2004, 1212-1220.
44. Fan XH, Sun K, Zhou XL, Zhang HM, Wu HY, Hui RT, Association of orthostatic hypertension and hypotension with target organ damage in middle and old-aged hypertensive patients. *Zhonghua Yi Xue Za Zhi*, 91:2011, 220-224.

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