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Review Article

Systematic Review: The Association between Late Life Depression and Hypotension

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A B S T R A C T

Background: Late life depression (LLD), defined as depressive illness in people aged 60 years or older, is more complex than depression presenting in earlier life, with different clinical features and a poorer response to therapy. Different biological factors underlie LLD and hypotension may be an important modifiable risk factor. The aim of this systematic review is to clarify the relationship between hypotension and LLD.

Methods: A systematic search was conducted in PubMed and Embase for articles published up to December 31, 2015. Key search terms were "depression," "depressive disorder," "hypotension," and "blood pressure." Studies were included if they were published as a primary research paper in a peer-reviewed journal, involved participants with a mean age of 60 years or more, and examined the relationship between hypotension and depression.

Results: The initial combined search retrieved 2268 nonduplicate articles. Of these, 116 full texts were assessed for eligibility, of which 19 were included in this systematic review.

Nine cross-sectional studies examined the association between hypotension and LLD, with 8/9 indicating a positive association between the 2. Five cross-sectional studies examined the relationship between orthostatic hypotension (OH) and LLD, with each study finding a positive association between the 2. Five longitudinal studies examined the relationship between hypotension and LLD, with discordant findings between studies. There were no longitudinal studies examining the relationship between OH and LLD.

Discussion: This systematic review found that cross-sectional studies demonstrated a consistent relationship between hypotension and LLD, but longitudinal data to date is less consistent, with discordant findings. There are several methodological limitations of published longitudinal data that may explain these differences, including differences in age at enrollment, depression and blood pressure assessment, and controlling for covariates.

Further longitudinal studies to clarify the role of these potentially modifiable factors in the development of this complex illness are essential.

One of the most welcome developments in our lifetime is that older people are now living significantly longer, healthier lives. The global share of older people (aged 60 years or over) increased from 9.2% 1990 to 11.7% in 2013, and the number of older people worldwide is expected to more than double, from 841 million people in 2013 to more than 2 billion by 2050.[1] The majority of these older people live independently. This represents one of the success stories of modern times; however, such marked demographic shifts do not come without significant challenges. One such challenge is the increasing prevalence of neuropsychiatric disorders of later life, including late life depression (LLD).

Given the strong vascular basis of LLD, one would expect to find a close relationship with blood pressure (BP) control and, in parallel, with dementia, there is an increasing body of evidence to suggest that hypotension may be an important factor in development of LLD. This review addresses the relationship between hypotension and depression in later life but in advance of that, we examine some important definitions and terminology surrounding both conditions.

LLD

LLD, defined as depressive illness with onset after 60 years or with onset before 60 years and persisting after the age of 60 years,[2] is common, especially in those with significant medical comorbidities and functional disability.[3] Depression can intensify these functional

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limitations,[4] and carries with it significant levels of morbidity and mortality,[5] as well as further functional limitations, independent of underlying illnesses.[6] The incidence of LLD ranges from 0.2 to 14.1 per 100 person-years for a major depressive episode and 6.8 per 100 person-years for a subclinical depressive episode,[7] with an estimated prevalence of 15% in people over 65 years.[8] In the Irish Longitudinal Study on Aging (TILDA), over 8% of a population-representative sample of older participants were found to have clinically relevant depressive symptoms on the Center for Epidemiologic Studies Depression Scale (CES-D).[9] With projected demographic changes, it is likely that the prevalence of depression in later life will increase significantly over the coming years and become an even more central public health issue.

Depression in older people is a more complex illness than depression presenting in earlier life.[10] Clinical features of LLD differ to earlier onset depression, with a higher likelihood of cognitive impairment, and executive dysfunction, which has been associated with a lower likelihood of remission of depressive symptoms.[11] In addition, underlying medical comorbidities, such as heart disease and frailty, add to this complexity. As well as intrinsic factors, extrinsic influences also contribute to this high prevalence of depressive illness in later life. Although later life is generally a time of reasonably good health and happiness, it is clear that it can also be a time of loss, bereavement, and social isolation for a minority of older people.

A meta-analysis has shown that after 24 months follow-up following the diagnosis of LLD, 50% of surviving participants remained depressed.[12] This is supported by a more recent longitudinal study demonstrating a chronic or relapsing course in approximately one-half of the cases diagnosed.[13] Suicide rates are higher among older adults than younger adults, and suicide is more closely associated with depression in this group.[10] Depression also tends to present differently in older adults, with less dysphoria and guilt, and more complaints of somatic symptoms, anhedonia, fatigue, sleep disturbance, and psychomotor retardation.[10]

A majority of research in this area concurs that LLD has a markedly different phenotype to depression occurring in earlier life. As well as the different social factors involved which confer vulnerability to low mood, it is also likely that different biological factors underlie depression in the older person. One such factor that has received much attention is the vascular basis of depression in later life, as well as the structural brain changes associated with this. This concept began to emerge when it was noted that patients with LLD had higher rates of cerebrovascular disease, reflected by cerebral white matter disease, than patients with earlier onset depression.[14] This has led to attempts to clarify the role played by vascular risk factors, such as BP, in the development of depression in later life.

Hypotension

Definition

There is no widely accepted definition of what value constitutes hypotension in the older patient, and instead of a “one size fits all” approach, BP targets are becoming increasingly individualized, considering both the age and fitness of the patient. International guidelines suggest that in general BP less than 120/80 mm Hg is “normal”[15] but in an older population there is an increasing trend toward less strict targets for BP control[16] and values of 140–150 mm Hg for systolic BP (SBP) may be considered optimal in certain circumstances in this setting.

The recent Systolic Blood Pressure Intervention Trial (SPRINT), however, demonstrated a reduction in cardiovascular deaths and vascular events combined in a subgroup of patients 75 years of age and over, and this may have important implications for lower therapeutic targets in older persons in subsequent BP guidelines,[17] despite concerns around the relatively strict exclusion criteria used.[18]

Furthermore, the cut-off values for hypotension are predominantly based on static BP values, and we must remain cognizant that BP is a highly dynamic variable, with significant variability and diurnal variation, which does not lend itself to the isolated measurements traditionally employed in clinical practice. When we consider that the heart beats over 100,000 times per day, the beat-to-beat variability of BP is such that these individual readings provide only a crude estimate of average overall BP.

Hypotensive syndromes

The term hypotension is broad and encompasses several hypotensive subtypes, with differing clinical features and relevance in the older person. Persistent hypotension is present both supine and standing and is best demonstrated on a 24-hour ambulatory BP monitor.

Orthostatic hypotension (OH) is defined as a drop in SBP by at least 20 mm Hg or diastolic BP (DBP) by at least 10 mm Hg within 3 minutes of standing, with or without symptoms of orthostatic intolerance. OH is further subclassified into initial OH, where symptoms occur within 30 seconds of standing; classic OH where symptoms occur between 30 seconds and 3 minutes from standing and delayed OH, with symptoms between 3 and 30 minutes after standing and characterized by a prolonged prodrome, frequently followed by sudden syncope.[19]

Postprandial hypotension (PPH) is defined as a as a drop of 20 mm Hg or more in SBP within 2 hours of the start of a meal or when the absolute level of SBP following a meal falls below 90 mm Hg where preprandial SBP is over 100 mm Hg.[20] It can occur both sitting and supine, more commonly after breakfast, and is thought to be related to an inability to compensate for hypotension caused by increased bowel blood flow after eating.[21]

BP measurement

The multiplicity of noninvasive techniques used to measure BP may also introduce inconsistency into study findings. Despite the technological advances in medical assessment over the last 100 years, the auscultatory method of BP measurement, using a sphygmomanometer remains in common use. The Korotkoff method continues to be the most widely used technique for measuring BP using a sphygmomanometer, but it tends to give values for systolic pressure that are lower than the true intra-arterial pressure, and diastolic values that are higher.[22] Findings are also operator-dependent and can be subject to inaccuracies such as terminal digit preference.[23]

The oscillometric method of BP measurement is commonly used in automated devices, including ambulatory BP monitors and is based on the finding that the point of maximal oscillation when deflating a sphygmomanometer cuff corresponds to the mean intra-arterial pressure. An algorithm is then used to determine SBP and DBP.[24] Theses algorithms are proprietary and differ from one another, meaning that commercial devices cannot be compared or standardized.[25] The oscillometric method requires less skill than the auscultatory method and cuff placement is less critical, however, there are concerns that automated measurement to BP, particularly DBP, in patients with arrhythmias such as atrial fibrillation may be inaccurate.[26]

Ambulatory BP is a fully automated BP recording, with multiple measurements over a defined period of time, usually 24 hours. During a typical monitoring session, BP is measured every 15 to 30 minutes over 24 hours including both awake and sleeping hours, ideally on a workday, with the total number of readings varying between 50 and 100.[27]

Noninvasive beat-to-beat BP is based on the vascular unloading technique.[28] It allows real-time continuous tracking of BP and gives waveform measurements similar to those seen in invasive intra-arterial monitoring.[29] It, therefore, captures dynamic BP shifts that are missed by other techniques and is of particular utility when