# Orthostatic Hypotension: clinical review and case study

## Introduction

This case study will reflect upon presenting dizziness and query, transient loss of consciousness (TLOC) in a 54 year old female patient with a background of long term depression (table 1). Following determination that the TLOC was non-traumatic and syncopal in nature (Brignole *et al,* 2018), differentials considered were; reflex syncope, which is a brief loss of consciousness due to a drop in blood pressure from a neurological cause, such as a vagsovagal, orthostatic hypotension, arrhythmia or other cardiovascular cause (Japp & Robertson, 2018; National Institute for Health and Care Excellence (NICE), 2014). A detailed record of the event, clinical history and examination including 12 lead electrocardiogram (ECG) (NICE, 2014) was conducted. No cardiac red flags were identified from the ECG, ruling out differentials of arrhythmia and other cardiac aetiologies (Japp & Robertson, 2018; Seller & Symons, 2012). A diagnosis of orthostatic hypotension (OH) was confirmed by a drop of systolic blood pressure greater than (>) 20mmHg and diastolic blood pressure >10mmHg within three minutes of standing (Freeman et al, 2011). The most likely underlying cause of OH in this case was considered to be iatrogenic (Gugger, 2011; Seller & Symons, 2012). Management of presenting OH was successfully treated through pharmacological optimisation (Freeman et al, 2011).

This article will discuss the causes of TLOC, focussing on orthostatic hypotension, its prevalence, presentation and causes and will reflect on the valuable role nurses have in to play in highlighting polypharmacy to doctors, and non-medical prescribers, as a contributing factor to orthostatic hypotension is polypharmacy. It is therefore vitally important to accurately distinguish TLOC aetiology, not only to provide appropriate management but to also identify patients at risk of morbidity/mortality related to underlying disease.

## Prevalence

TLOC accounts for 3% of all attendance in emergency departments within the United Kingdom (UK) (Petkar, Cooper & Fitzpatrick, 2006) and has a lifetime prevalence of 50% (National Institute for Health and Care Excellence (NICE), 2014). Data shows vast international differences in admission rates of patients presenting with TLOC,

varying between 12% in Canada (Thiruganasambandamoorthy et al, 2013) and 86% in the United States of America (Birnbaum et al, 2008). A study in the UK reports a 49% rate of admission with subsequent one month cause of death or serious outcome occurring in 7.3% of patients (Reed et al, 2010).

## Presentation

More than 90% of TLOC presentations are due to epileptic seizures, psychogenic seizures or syncope (Reuber et al, 2016). In England and Wales it has been estimated that 92,000 patients were incorrectly diagnosed with epilepsy in 2002 (Juarez-Garcia et al, 2006). A misdiagnosis of epilepsy is estimated at an annual cost of additional healthcare of up to £189 million (NICE, 2004). It is therefore vitally important to accurately distinguish TLOC aetiology, not only to provide appropriate management but to also identify patients at risk of morbidity/mortality related to underlying disease (Petkar, Cooper & Fitzpatrick, 2006; Reuber et al, 2016). The development of evidence based, clinical guidance (NICE, 2014; Van Dijk et al, 2008; Wardrope Newberry & Reuber, 2018) seeks to reduce incidence of misdiagnosis in TLOC, improve patient outcomes and enhance cost effective care. However in a recent systematic review it was concluded that there remains a lack of validated diagnostic criteria to differentiate between causes of TLOC (Wardrope, Newberry & Reuber, 2018).

## Orthostatic hypotension

Studies reveal that presenting syncope is often unexplained (Olde Nordkamp et al, 2009; Soteriades et al, 2002) with the most likely diagnosis being reflex syncope in patients less than (<) 60 years old (Del Rosso et al, 2005). The second most common cause of syncope is OH, occurring in approximately 15% of syncopal presentations (Sutton, 2013). A recent meta-analysis suggests that OH is highly prevalent, affecting nearly one in five older adults (>60 years) living in the community and almost one in four older adults (>60 years) living in long term care (Saedon, Tan & Frith, 2018). Presence of OH is independently associated with predicting all-cause mortality (Ricci et al, 2015; Sasaki et al, 2005; Weiss et al, 2006), incidence of cardiovascular disease (Fagard & De Cort, 2010; Ricci et al, 2015; Verwoert et al, 2008) and increased risk of major adverse cerebro-cardiovascular events (Hossain et al, 2001; Ricci et al, 2015). Unexpectedly and relevant in this case, a recent meta-analysis demonstrates a greater association between OH and all-cause death in individuals under 65 years old (Ricci

et al, 2015). Similarly, Rose et al (2006) found that relative risk of stroke predicted by OH decreases with advancing age. OH is found to be more prevalent in hypertensive women, irrespective of treatment status (Kamaruzzaman et al, 2009). However, the varied heterogeneity of prevalence studies and variance in diagnostic assessment, provides an unclear picture (Frith & Parry, 2017; Lahrmann et al, 2005).

In relation to this case study, the patient was female and past medical history revealed hypertension, in which she was prescribed Amlodipine 5mg once daily. Nursing staff found the patient on the floor and had stated that she had been experiencing light headedness and dizziness for a few days prior to this incident but had not collapsed previously.

## Causes

OH is a common cardiovascular disorder which can be idiopathic or occur as a result of an underlying neurodegenerative disease, blood loss, dehydration, or antihypertensive medication use, as prescribed in this case study (Gibbons et al, 2010; Lahrmann et al, 2006; Ricci, De Caterina & Fedorowski, 2015). It is symptomatic of a structural or functional autonomic nervous system (ANS) failure, typically occurring when cardiovascular adaptive mechanisms fail to adequately compensate for the reduction in venous return that normally happens on moving to an upright position (Goldstein et al, 2002; Ricci, De Caterina & Fedorowski, 2015). Orthostatic stress presents an ongoing challenge for the body, given that people often alter their posture between recumbent and upright positions regularly throughout the day. Kanjwal et al (2015) report that orthostatic stabilisation is normally achieved within one minute of standing. However, when homeostatic mechanisms fail, this results in a transient or persistent state of hypotension, which in turn can lead to syncope inducing a loss of consciousness (Fedorowski & Melander, 2013; Naschitz & Rosner, 2007; Ricci, De Caterina & Fedorowski, 2015).

## Regulation of blood pressure

Normal regulation of blood pressure (BP) occurs via a range of physiological actions of the cardiovascular, neural, renal and endocrine systems (Chopra, Baby & Jacob, 2011). Immediately upon assuming an upright stance, a gravitational displacement of approximately 500 millilitres of blood moves away from the thorax to the distensible venous capacitance system below the diaphragm known as venous pooling. Venous

return is temporarily reduced resulting in a decrease in cardiac stroke volume, reduced arterial BP and an immediate decline in blood flow to the brain (Olufsen et al, 2005). When the brain is insufficiently supplied with oxygenated blood referred to as cerebral hypoperfusion, this manifests as feeling dizzy or lightheaded (Fedorowski & Melander, 2013; Serrador, 2019). This was the prodromal presenting symptom of this case study, experienced over a period of a few days prior to incidence of syncope.

The reduction in systemic arterial BP is detected by the distensible baroreceptors located in the carotid and aortic walls, noting change in the tension of the arterial walls (Gugger, 2011). Consequently, the ANS which is responsible for mediated changes in cardiac output and vascular tone to maintain BP homeostasis (Dampney et al, 2002; Ricci, De Caterina & Fedorowski, 2015), responds in two ways; parasympathetic withdrawal and sympathetic activation of the baroreflex-mediated autonomic regulation. Parasympathetic withdrawal is understood to induce a rapid increase in heart rate via its negative chronotropic and inotropic effects (Ripplinger, Noujaim & Linz, 2016). Whereas the sympathetic nervous system activates a slower increase in vascular resistance, vascular tone and cardiac contractility, increasing heart rate (Gordan, Gwathmey & Xie, 2015). Concurrently, cerebral autoregulation, which is the ability of the brain to maintain cerebral blood flow to keep the brain perfused, maintains cerebral blood flow via a combination of neurogenic processes, myogenic tone and metabolic demand (Serrador, 2019).

**Hydrostatic indifference point**

The reference point for where pressure is independent of posture, is referred to as the venous hydrostatic indifference point (HIP) (Tortora & Derrickson, 2011). The HIP is considered to denote the circulatory balance between hydrostatic pressure and vasomotor activity. However, is considered to underestimate the gravitational influence on blood volume distribution (Peterson et al, 2014). The venous system hosts approximately 70% of the total blood volume with adjustable capacity according to haemodynamic conditions (Aya & Cecconi, 2019; Ricci, De Caterina & Fedorowski, 2015). Given that blood arrives in the venous system for transportation via the connective capillary system, venous return is determined to a certain degree by the regulation of capillary circulation. Every tissue within the body has a rapid response regulatory system governed by metabolic need to provide adequate localised blood

flow (Aya & Cecconi, 2019). Haemodynamic stability is therefore directly influenced by the complexities of systemic circulation (Martini, Bartholomew & Ober, 2015).

The anatomy and physiology, can provide important insights into previously noted pathophysiological links between OH and negative outcomes (Fagard & De Cort, 2010; Hossain et al, 2001; Ricci et al, 2015; Sasaki et al, 2005; Verwoert et al, 2008; Weiss et al, 2006). For example, the presence of higher diurnal variability and supine, nocturnal hypertension in OH, may increase the risk of myocardial ischaemia and congestive heart failure as a result of intermittent episodes of increased afterload (Ricci, De Caterina & Fedorowski, 2015). Additionally, cerebrovascular or cardiovascular events can occur as a sequential product of orthostatic, neuroendocrine compensatory mechanisms, which try to maintain cardiac output but can over activate causing other biological effectors such as platelet formation and the coagulation cascade (Ricci, De Caterina & Fedorowski, 2015).

**Importance of clinical history**

Ascertaining an accurate clinical history (appendix 1) and sequential description of presenting symptoms has high diagnostic value in OH (Freeman et al, 2011; Lahrmann et al, 2006). This presenting case of potential TLOC is complicated by the fact that the event had resolved itself at the time of assessment (Japp & Robertson, 2018). This alongside, the absence of a witness to corroborate information related to experience of TLOC somewhat presents a diagnostic challenge (NICE, 2014). Staff found the patient sitting on the floor, fully conscious as denoted using the updated 'Glasgow Coma Scale' (Teasdale et al., 2014). The patient reported having felt dizzy upon getting up from her bed and walking a short distance to then find herself slumped on the floor, believing to have fainted. On the basis of this information and evidential loss of muscle control, guidelines indicate that TLOC must be assumed (Japp & Robertson, 2018; Whinnery & Forster, 2017).

Van Dijk et al, (2008) advocate that gathering an accurate clinical history can differentiate syncope from other forms of TLOC, including cardiac causes (Berecki-Gisolf et al, 2013). Nurses play an important role if they witness syncope in a patient, as important information may be relayed to doctors to assist in the correct diagnosis and treatment of the syncope. Reuber et al. (2016) explored the diagnostic potential of a self-reporting questionnaire to differentiate TLOC cause. They concluded that

clusters of self-reported symptoms can be effective in directing appropriate pathways of investigation and treatment. In regards to this case study, upon review of the 86 item Paroxysmal Event Profile questionnaire, feeling “light headed” in the prodromal phase, no recall of falling during the event and mild, temporary confusion post episode as in this case, is more consistent with a syncopal explanation of TLOC as opposed to epilepsy or psychogenic seizure. Given that potential adverse events are determined by the acute underlying disease as opposed to the syncope itself, accurate diagnosis is crucial (Numeroso et al, 2016).

## Risk stratification tools

Reed et al, (2010) propose a risk stratification protocol for presenting syncope, denoted as the ‘ROSE’ rule aided by mnemonic BRACES (appendix 1). They claim that use of this simple clinical decision aide is practical and will potentially reduce the number of unnecessary admissions. Part application of this tool, identified no clinical markers indicative of a transfer to the emergency department for admission (table 1 1). However, Brignole et al, (2018) cautions against using syncope risk stratification strategies independent of clinical judgement due to no significant evidence of superiority in terms of predicting outcomes. The defining characteristics of syncope are; low BP and cerebral hypoperfusion, as a result of low peripheral resistance and/or reduced cardiac output (Brignole et al, 2014). In this case, the patient experienced no associated chest pain, new onset dyspnoea, family or personal history of cardiac disease, aside from hypertension (NICE, 2014; Reed et al, 2010). This alongside the absence of abnormalities on ECG and blood tests, allows safe dismissal of arrhythmia and cardiac syncope (Berecki-Gisolf et al, 2013; Brignole et al, 2014; Del Rosso et al, 2008; Reed et al, 2010). Despite reflex syncope being the most common cause of TLOC in patients <60 years old (Del Rosso, 2005), this differential diagnosis was ruled out on the basis of incomparable prodromal and clinical features (appendix 1; Brignole et al, 2014; Wieling et al, 2009).

On further examination, a diagnosis of OH was confirmed in this case by a drop in systolic BP of >20mm Hg and diastolic BP of >10mm Hg within three minutes of standing (Freeman, et al, 2011). As previously discussed OH is a common cardiovascular disorder which has been shown to have a greater association with all

cause death in patients <65 years old (Ricci, De Caterina & Fedorowski, 2015). Identification of the underlying cause in this case is therefore vital. On examination there was no evidence of injury or blood loss and the inpatient nutritional chart indicated the patient was sufficiently hydrated, therefore causative hypovolaemia was not considered to be a factor (Gibbons et al, 2010; Lahrmann et al, 2006).

**Importance of medication history and review**

A key consideration in this patient's medication history is secondary prescribing; her GP managed her hypertensive medication and she saw a private psychiatrist for psychotropic medication management. She was admitted to an NHS acute psychiatric ward, due to presenting risks to self in the form of suicidal ideation. On admission, contact was made with the private psychiatrist who shared clinical reasoning for the commencement of a monoamine oxidase inhibitor (MAOI) and his plan for titration of Phenalzine the selected MAOI in this case. Given presenting history of chronic depression, the plan in isolation made good sense, however it is not clear if the risk/benefit balance was considered in combination with prescribed antihypertensive and anti-psychotic medication (Duerden, Avery & Payne, 2013). Monitoring of BP is a requirement for patients prescribed Phenalzine (Joint Formulary Committee, 2018), unfortunately the patient's records did not reflect regular monitoring. Staff acknowledged that they were unfamiliar with prescribing and monitoring of MAOIs. However, the physical health monitoring of mental health patients is a core component of delivering safe and effective healthcare (NHS England, 2018). Furthermore, given that the patient was owed a duty of care it could be argued that potentially foreseeable harm was caused by omission of, due consideration of prescribing plan and inadequate monitoring (Caparo v Dickman, 1990; Donoghue v Stephenson, 1932). In this case professional duty of candour (General Medical Council & Nursing & Midwifery Council, 2015) was applied, see below for content of conversation with the patient and her husband.

In iatrogenic autonomic failure, reflex responses are compromised by drugs that reduce systemic vascular resistance (Hopson, Rea & Kienzle, 1993), causing syncope secondary to OH (Brignole et al, 2018). Meyer (2018) argues that the titration of MAOI's is balanced upon tolerability probabilities with orthostasis the primary dose limiting adverse effect. It is understood that rapid titration of a MAOI is not advised in

older individuals or those prescribed a α1-adrenergic antagonist such as Quetiapine (Electronic Medicines Compendium, 2018), which is associated with high incidence of OH (McEvoy et al, 2006). Anecdotal evidence would suggest that the presenting mental health condition with associated risk of suicide was the primary focus for staff, which may have influenced a faster titration regime than was considered safe, when taking into consideration the risk of adverse effects. The medication history of this patient (table 1) is of great importance in relation to the cumulative effects of prescribed medication on vascular resistance in this case of presenting OH (Gugger, 2011). The key clinical feature indicative of syncope due to OH as evidenced in this case study is the temporal relationship, with onset of syncopal symptoms and recent increase in prescribed vasodepressive medication, (Brignole et al, 2018) namely Phenalzine. Knowledge and understanding of medication interactions can present a challenge, the gravity of such highlighted by Freeman et al, (2011) who report that over 250 medications cause OH.

Remarkably, the advisory goal of OH treatment is focussed on improving functional capacity and quality of life, and preventing injury as opposed to achieving a target BP (Lahrmann et al, 2006). As previously discussed the guidelines for the management of TLOC, syncopal in nature is underpinned by risk assessment (Brignole et al, 2018). Given the numerous variables in aetiology, presenting symptoms and associated co-morbidities, successful treatment of OH is unsurprisingly a challenge (Ejaz et al, 2004).

On confirmation of OH, the patient and her husband were provided with information and advice on factors that influence BP (Lahrmann et al, 2006). It is important for nurses to know what advice to give to patients, carers and loved ones as the patient and carer education is considered central to treatment efficacy, with a focus on promoting understanding of basic physiology, identifying aggravating factors and learning how to reduce incidence of decreased BP (Benditt & Nguyen, 2009; Wieling et al, 2015). Advice given included staged, slow change in position from supine to standing and repeated contraction of lower leg muscles before and whilst standing (Brignole et al, 2018). The patient was subsequently able to recognise early warning signs in relation to haemodynamic changes, which provided an opportunity for her to implement physical countermeasures in a timely manner, reducing risk of syncope and injury (Ricci et al, 2015).

## De-prescribing

Whilst non-pharmacological treatment intervention in the form of prescribing was indicated in this case, given concern related to medication plan, de-prescribing was considered at length. International guidance and expert consensus recommend the withdrawal of medication in OH, with specific focus on six classes of medication including vasodilators, antihypertensives and antidepressants particularly tricyclics including MAOIs (Freeman et al, 2011; Lahrmann et al, 2006). However, Frith & Parry (2017) report evidential inconsistencies in withdrawing causative medication, further acknowledging that complex variables in methodological, clinical and statistical heterogeneity creates problems in drawing comparative conclusions. In this case, prescribed medication for previous hypertension was withdrawn and the patient noted a reduction in dizziness after one week. She experienced no further episode of syncope and her blood pressure returned to within a normal range. She went on to make a reasonable recovery in mental health and is having regular BP monitoring from her GP.

## Conclusion

In conclusion, this case study reflects a critical review of the assessment, diagnosis and treatment of a female inpatient presenting with syncope. Given the numerous variables in aetiology, presenting symptoms and associated co-morbidities, successful treatment of OH is unsurprisingly a challenge (Ejaz et al, 2004). Nurses have a valuable role in being able to describe the type of syncope to doctors, if witnessed, as this can assist with the diagnosis and treatment. With regards to this case study a diagnosis of OH was confirmed with prescribed medication considered to be the most likely aetiological factor, again highlighting that nurses are often best placed to act as the patient's advocate and flag polypharmacy as a potential cause of OH. Medicines optimisation provided successful treatment, as well as advice no further incidence of syncope occurred and the patient suffered no lasting effects from the adverse event. The patient and her husband were given informed advice on how to reduce the incidence of postural hypotension, emphasising the importance of nurses understanding the pathophysiology, the causes and aggravating factors of OH.

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