BLACKOUT/SYNCOPE
Supporting information

This guideline has been prepared with reference to the following:

NICE. Transient loss of consciousness ('blackouts') in over 16s. 2023. London. NICE

https://www.nice.org.uk/guidance/cg109

NICE. Suspected neurological conditions: recognition and referral. 2023. London. NICE

https://www.nice.org.uk/guidance/ng127

Brignole M, Moya A, de Lange FJ et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J. 2018;39:1883-48

https://academic.oup.com/eurheartj/article/39/21/1883/4939241

What are the risks and benefits of drug therapy for neurally mediated reflex syncope?
Fludrocortisone in a RCT showed a nonsignificant 31% reduction in syncope recurrence (p = .069), and in an exploratory analysis, a dose of 0.2 mg significantly reduced syncope recurrence (p = .019) [Sheldon, 2016]
Various small studies and a systematic review have shown some benefits of midodrine in VVS. POST 4 trial is a randomized, placebo controlled trial that assessed midodrine's benefit in reducing syncope recurrence in vasovagal syncope. Midodrine at a dose of up to 10 mg, three times daily, was associated with a 1-year actuarial syncope rate of 46% versus 67% in the placebo group (p = .03) [Sheldon, 2021]. The number needed to treat with midodrine to prevent one patient from having syncope was five. Midodrine was associated with a relative risk of syncope recurrence of 0.69 (CI, 0.49–0.97; p = .035).
Multicentre, double-blind, randomized trials have reported that the beta-blockers are no more effective than placebo in preventing syncope recurrence (Sheldon 2006 & Madrid 2001). However, a meta-analysis of the POST study and a large observational study showed that beta-blockers decrease the syncope recurrence by 48% in patients ≥42 years, but in patients <42 years of age, the risk of recurrence is increased by 58% (Sheldon, 2012).
Serotonin reuptake inhibitors (e.g., paroxetine) and norepinephrine transporter inhibitors (e.g., reboxetine, sibutramine, atomoxetine) have also been used in VVS, but the data to support their significant benefit is lacking (Di Girolamo 1999 & Lei, 2020).
A Cochrane review of 46 studies (Romme, 2011) concluded that: "There is insufficient evidence to support the use of any of the pharmacological or pacemaker treatments for vasovagal syncope and carotid sinus syncope. Larger studies using patient relevant outcomes are needed." The 2018 guidelines from European Society of Cariology similarly concluded that "many drugs have been tested in the treatment of reflex syncope, for the most part with disappointing results (Brignole, 2018). While results have been satisfactory in uncontrolled trials or short-term controlled trials, several long-term placebo-controlled prospective trials have not shown a benefit of the active drug over placebo, with some exceptions".

Brignole M, Moya A, de Lange FJ et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J. 2018;39:1883-948
https://academic.oup.com/eurheartj/article/39/21/1883/4939241

Di Girolamo E, Di Iorio C, Sabatini P et al. Effects of paroxetine hydrochloride, a selective serotonin reuptake inhibitor, on refractory vasovagal syncope: a randomized, double blind, placebo-controlled study. J Am Coll Cardiol. 1999;33:1227-30
https://linkinghub.elsevier.com/retrieve/pii/S0735-1097(98)00694-9

Lei LY, Raj SR, Sheldon RS. Pharmacological norepinephrine transporter inhibition for the prevention of vasovagal syncope in young and adult subjects: a systematic review and meta-analysis. Heart Rhythm. 2020;17:8
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7335357/

Madrid AH, Ortega J, Rebollo JG, et al. Lack of efficacy of atenolol for the prevention of neurally mediated syncope in a highly symptomatic population: a prospective, double-blind, randomized and placebo controlled study. J Am Coll Cardiol. 2001;37:554-9
https://linkinghub.elsevier.com/retrieve/pii/S0735-1097(00)01155-4

Romme JJ, Reitsma JB, Black CN, et al. Drugs and pacemakers for vasovagal, carotid sinus and situational syncope. Cochrane Database Syst Rev. 2011, Issue 10. Art. No.: CD004194
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004194.pub3/full

Sheldon R, Raj SR, Rose MS, et al. Fludrocortisone for the prevention of vasovagal syncope. J Am Coll Cardiol. 2016;68:1-9
https://linkinghub.elsevier.com/retrieve/pii/S0735-1097(16)32934-5

Sheldon R, Faris P, Tang A, et al. Midodrine for the prevention of vasovagal syncope: a randomized clinical trial. Ann Intern Med. 2021:1-9

Sheldon R, Connolly S, Rose S, et al. Prevention of syncope trial (POST): a randomized, placebo-controlled study of metoprolol in the prevention of vasovagal syncope. Circulation. 2006;113:1164-70

Sheldon RS, Morillo CA, Klingenheben T et al. Age-dependent effect of β-blockers in preventing vasovagal syncope. Circ Arrhythm Electrophysiol. 2012;5:920-26

Evidence Level: I

Older patients suffering from syncope who have abnormal ECG readings?

Marrison (2012) identifies a number of conditions among elderly patients leading to abnormal ECG readings which could increase clinical risk. These include “Left bundle branch block or right bundle branch block, Asymptomatic inappropriate sinus bradycardia (< 50 bpm); Sinus pauses ≥ 3 s; Chronotropic incompetence; Mobitz 1 atrioventricular block; Pre-excited QRS complexes; Prolonged corrected QT interval and Very prolonged PR interval.” These require further investigation.

Marrison VK, Fletcher A and Parry SW. The older patient with syncope: Practicalities and controversies. International Journal of Cardiology, 2012;155 (1): 9-13

Evidence Level: V

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