J Cardiovasc Disease Res., 2017; 8(3):66-71
A Multifaceted Peer Reviewed Journal in the field of Cardiology
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Review Article

Laughter-Induced Syncope: Literature Review

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ABSTRACT
Syncope is a common and pervasive medical problem. The etiology of 30-40% of syncope remains unknown. Laughter-induced syncope is a rare subtype of vasovagal syncope that is not well understood. With this literature review we hope to elucidate the epidemiology, symptomatology, pathophysiology, diagnosis and therapeutic options of laughter-induced syncope. Greater awareness of laughter-induced syncope may better direct clinical investigations and improve patient care.
Keywords: Laughter-induced syncope, Situational syncope, Gelastic syncope, Sitcom syncope, Syncope.

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Submission Date: 18-02-2016;
Revision Date: 19-05-2016;
Accepted Date: 11-06-2016.
DOI : 10.5530/jcdr.2017.3.17

INTRODUCTION

Syncope is defined as an acute loss of consciousness secondary to brief global cerebral hypoperfusion associated with a lack of ability to maintain postural control. Episodes of syncope are sudden in onset, transient, and occur with full spontaneous recovery.[1] The prevalence is similar between genders (30–50%), increasing proportionally with age and accompanied by a sharp rise in prevalence after the age of 70.[2,3] Syncope represents 3–5% of emergency department visits.[3] Of those people presenting to the emergency department for syncope, 40% of patients are subsequently admitted.[4]

Causes of syncope can be categorized into vasovagal (21.2%), stroke (4.1%), seizure (4.9%), orthostatic (9.4%), cardiac (9.5%), medication (6.8%), unknown (36.6%) and situational syncopes (7.5%).[2] When reflex-mediated syncope occurs in conditions that precipitate the Valsalva maneuver, such as laughing, carrying weight, defecation, or coughing, it is called situational syncope. Only around 8% of all syncope is situational. Laughter-induced syncope is a rare subtype of situational syncope and there have been only a few cases described in literature.

Laughter-induced syncope is also called gelastic syncope, from the Greek word "gelastikos" or "able to laugh". The first published case report of laughter-induced syncope was by Cox *et al*. in 1997.[5] The patient had a brachiocephalic stenosis and lost consciousness while watching Seinfeld. From then on, laughter syncope was also known as "Seinfeld syncope" or "Sitcom syncope". To the best of our knowledge, there are about 19 cases of laughter-induced syncope published in literature. Case reports on laughter-induced syncope are summarized on Table 1.

Some of the patients, similar to the case by Cox and colleagues, have underlying medical conditions that contributed to the syncope, such as ependymoma or Takayasu's arteritis.[5] Most cases are reported to occur in the elderly or in those with co-morbidities such as diabetes mellitus and coronary artery disease. In only in a few instances has laughter-induced syncope involved young and healthy individuals. History taking is the basis of diagnosing patients who present with syncope. This is especially true in patients with situational syncope. Although there is currently no diagnostic gold standard, history, physical exam and electrocardiography have a combined diagnostic yield of 50% in determining the etiology of syncope.[6] A strong temporal relationship between the triggering events and the syncopal episodes supports a diagnosis of situational syncope. For laughter-induced syncope, history will reveal vigorous laughter immediately prior to the syncope. It always involves a brief loss of consciousness with quick resolution of symptoms.

Previous case reports showed that laughter-induced syncope happens infrequently (Table 1). Although two of the patients have episodes of more than five times, patients usually only have 3-5 prior episodes of syncope before being diagnosed. Many only have one reported episode. Lightheadedness, dizziness, visual blurring or darkening of visual field may sometimes accompany these laughter-induced syncopes. Two patients with an underlying carotid artery and brachiocephalic stenoses described an associated amarausis fugax. These symptoms are non-specific, but when such prodromal symptoms are present, patients can try to avoid the ensuing syncope by curtailing their laughter. In our patient, his prior episodes were only pre-syncopal. There is some lightheadedness, but he is otherwise asymptomatic.

Diagnostic tests do not play a major role in diagnosing situational syncopes. They are usually used to rule-out underlying cardiac or neurologic causes of syncope. They are also done to determine if there are other underlying etiologies or reversible causes. For laughter-induced syncope, diagnostic tests are commonly negative. In the literature, the ECGs of the reported cases were mostly normal. There are no predominant brady-arrhythmias or tachyarrhythmias. Holter monitoring was done in eight of them to detect underlying arrhythmias and the results were negative. Echocardiograms would predominantly be normal. The results of cardiac stress tests in the literature have been negative for ischemia except for one patient.

Tilt testing is a diagnostic adjunct that is commonly employed in vasovagal syncope and its subtypes. For laughter syncope patients who underwent tilt table testing, results have been positive. Loss of consciousness, a drop in blood pressure or a change in heart rate has been elicited during tilt table testing in some of the patients.

In the review of literature, coronary angiography was employed in one patient with laughter-induced syncope. Its results revealed no significant coronary artery disease. If there is suspicion for an arrhythmogenic cause of syncope, an electrophysiology (EP) study is sometimes also done to rule it out. No previous case reports have done an EP study on a patient with laughter-induced syncope.

The Bezold-Jarisch Reflex has been proposed to explain the mechanism behind laughter-induced syncope. Intense laughter causes episodes of prolonged forced expiration against a closed glottis, resulting in de-

Table 1: **Results of literature review on laughter syncope.**

Authors and Year of Publication	Age, Sex, and Medical Condition	Prodrome	No. of Syncope	ECG/ Holter	2D-Echo/ Cardiac Stress Test	Tilt Table Test	Angiography	CT/MRI Brain	Other Studies	Treatment	Outcome
1997 (Cox *et al.*)[5]	62 y.o./Male Smoking Hypertension Dyslipidemia CABG* history Predisposing factor: Bilateral carotid disease and brachicephalic stenosis	Monocular Blindness	3	-/-	-/-	-	70% left external carotid stenosis, 40% left subclavian stenosis, and 90% stenosis of brachiocephalic trunk	-	-	Percutaneous stenting	No recurrence
2002 (Totah and Benbadis).[9]	55 y.o./Male Obesity	-	2	N/-	-/-	-	Coronary angiogram: no abnormalities	N (CT brain)	Sleep study: Mild to moderate obstructive sleep apnea	-	-
2005 (Bloomfield and Jazrawi).[10]	32 y.o./Male None	-	1	N	-/-	-	-	N (MRI brain)		None	No recurrence after 2 years of follow up
2005 (Braga *et al.*)[11]	63 y.o./Male Type II diabetes mellitus	Blurred vision Lightheadedness	10	N/-	-/-	Mix vasovagal syncope was induced	-	-		-	-

2006 (Amaki *et al.*)[12]	69 y.o./Male None	-	6	N/N	Mild mitral regurgitation/ Dipyridamole imaging-negative	Positive with Isoproterenol infusion	-	N (CT brain)	Carotid artery USG: normal	Propranolol and Midodrine	No recurrence
2006 (Bragg)[13]	60 y.o./Male Ex-smoker	Blurred vision Lightheadedness Weakness	3	N/-	-/-	-	-	-	-	-	-
2006 (Lo and Cohen)[14]	29 y.o./Male None	Lightheadedness Dizziness	1	N/-	N/-	Positive for neurocardiogranic syncope	-	-	-	-	-
2007 (Famularo *et al.*)[15]	53 y.o./Male Predisposing factor: Ependymoma	-	3	N/-	N/-	Lost consciousness for 5 mins and BP and HR dropped	-	Cerebellar vermis tumor abutting floor of fourth ventricle	-	Surgical resection of tumor (Histological examination: ependymoma)	No recurrence
2007 (Nishida *et al.*)[16]	56 y.o./Male Obstructive sleep apnea Hypertension Hyperlipidemia	Short of breath Darkening of surroundings	1	-/-	-/Treadmill stress test: negative	-	-	-	-	-	-
2009 (Awada *et al*)[17]	63 y.o./Male Hypertension Diabetes Peripheral neuropathy Lacunar pseudobulbar palsy	-	3	N/N	-/-	-	-	MRI: Bilateral lacunar infarctions	-	Bisoprolol	No recurrence
2009 (Gullapalli *et al.*)[18]	67 y.o./Male None	Blurring of vision Darkening of visual field Feeling faint	-	-/-	-/-	-	-	MRI: Mild periventricular changes (N)	Carotid artery USG: normal	Behavioral modification	No recurrence

2010 (Shah and Gerber)[19]	29 y.o./Female Hypertension Obesity Hypothyroidism Nephrotic syndrome Predisposing factor: Takayasu's Arteritis	Amaurosis fugax	1	-/-	EF 65% with moderate aortic regurgitation/-	-	Stenosis of the bilateral carotid and subclavian arteries and extensive occlusions of the great vessels of the aortic arch	MRI: Mild dilatation of the ascending aorta, and marked narrowing of the bilateral common carotid and subclavian arteries	Carotid artery USG: No demonstrable flow in the left common carotid artery, narrowed left subclavian and axillary arteries, and a markedly narrowed right common carotid artery with wall thick ening	Methylprednisolone 1 gram daily for 3 days (for Takayasu arteritis) Ascending aorta-to-left carotid artery bifurcation bypass procedure	No recurrence
2010 (Thiagarajah *et al*)[20]	74 y.o./Male Not mentioned	-	5	N/N	Moderate aortic regurgitation/ Stress test: N	Positive (BP and HR decreased) with loss of consciousness	-	-	Carotid artery USG: normal	Adequate hydration and avoidance of dehydration and prolonged standing	No recurrence
	51 y.o./Male Not mentioned	Lightheadedness	1	Left anterior fascicular block/N	Dilated left atrium, normal left ventricular size/Stress test: N	Positive (BP dropped)	-	-	Carotid artery USG: normal	Curtailing laughter	No recurrence
	57 y.o./Female Coronary artery disease with stents to the left anterior descending and left circumflex arteries	-	1	N/N	Trace mitral regurgitation and trace tricuspid regurgitation/ Stress echo: Apical inferolateral hypokinesia	Positive (BP dropped and HR elevated)	-	-	Carotid artery USG: normal	Curtailing laughter	No recurrence
2012 (Otmani *et al.*)[21]	65 y.o./Male No significant medical condition	-	4	N/-	N/-	-	-	N (MRI)	-	Propranolol	No recurrence

2012 (Gaitatzis and Petzold)[22]	42 y.o./Male None	None	Multiple episodes	N/-	-/-	-	-	N (MRI)	-	-	-
2012 (Patel *et al.*)[23]	54 y.o./Male Diabetes mellitus Hypertension	Lightheadedness and blurring of vision	4	N/N	N/-	N		N	Carotid artery USG: normal Sleep study: OSA	Auto-CPAP at night time Weight reduction Exercise	-
2013 (Haddad *et al.*)[24]	58 y.o./Male None	No prodrome; only weakness after the episodes	3	-/N	N/N	N	-	N	-	-	-

*CABG- coronary artery bypass graft; *N-normal; *EF-ejection fraction

creased lung volume and elevated intrathoracic pressure. The increase in intrathoracic pressure, decreases venous return to the heart, activating baroreceptors that inturn reduce sympathetic activity and heighten parasympathetic cardiovascular tone. These lead to hypotension and bradycardia that result in sudden cerebrovascular hypo perfusion and subsequent loss of consciousness.[7]

The treatment of situational syncope mostly involves avoidance of triggers or instances that elicit the transient loss of consciousness. It also involves identifying prodromal symptoms and adapting protective postures such as being in a supine position with legs raised. Maneuvers can also be employed to try to halt the attacks through physical counter-pressure measures such as tensing the arms with clenched fists and leg crossing. Being a subtype of vasovagal syncope, laughter-induced syncope is medically managed in the same way as vasovagal syncope. Of all the interventions, there is currently no available evidence to support any form of treatment employed for vasovagal syncope. Support stockings, volume expansion through liberal fluid and salt intake, beta-blockers and, the vasopressor, midodrine are commonly employed. These measures may ameliorate the frequency of syncope, however, sufficient evidence to support them are lacking.[1-8]

In laughter-induced syncope cases found in literature, the most common therapy employed is advising patients to curtail their laughter. For those who have contributing medical illness, addressing the underlying problem has been curative. Examples are stenting of brachiocephalic stenosis, surgical resection of ependymoma, and bypass of carotid stenosis. Reflex-mediated syncopes like laughter syncope are benign. Unless there is an underlying cardiac or neurologic abnormality, patients are healthy and have good prognosis.

CONCLUSION

In conclusion, a large number of episodes of syncope have an unknown etiology. History, physical exam and ECG are important for arriving at a diagnosis. Cardiac evaluation is useful in ruling-out cardiac causes that might suggest a poor prognosis. Situational syncope can be diagnosed by history alone and investigational tests usually yield negative results.

AUTHOR CONTRIBUTIONS

Biso S, Wongrakpanich S, Agrawal A, Yadlapati S, Kishlyansky M and De Venecia T all contributed to the literature review and writing of the manuscript.

ACKNOWLEDGEMENT

The authors would like to thank Dr. Chitra Punjabi at Einstein Medical Center, Philadelphia, Pennsylvania, for assistance with article preparation.

ABBREVIATIONS USED

*CABG- coronary artery bypass graft; *N-normal; *EF-ejection fraction.

REFERENCES

1. Moya A, Sutton R, Ammirati F, Blanc JJ, Brignole M, *et al.* Guidelines for the diagnosis and management of syncope (version 2009). European heart journal. 2009;30(21):2631-71.
2. Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, *et al.* Incidence and prognosis of syncope. New England Journal of Medicine. 2002;347(12):878-85.
3. Manolis AS, Linzer M, Salem D, Estes NM. Syncope: current diagnostic evaluation and management. Annals of Internal Medicine. 1990;112(11):850-63.
4. D'Ascenzo F, Biondi-Zoccai G, Reed MJ, Gabayan GZ, Suzuki M, *et al.* Incidence, etiology and predictors of adverse outcomes in 43,315 patients presenting to the Emergency Department with syncope: an international meta-analysis. International journal of cardiology. 2013;167(1):57-62.
5. Cox SV, Eisenhauer EC, Hreib K. "Seinfeld syncope," Cathet Cardiovasc Diagn.

1997;42(2):242
6. Linzer M, Yang EH, Estes NM, Wang P, Vorperian VR, *et al.* Clinical guideline: diagnosing syncope: part 1: value of history, physical examination, and electrocardiography. Annals of Internal Medicine. 1997;126(12):989-96.
7. Da Silva RM. Syncope: epidemiology, etiology, and prognosis. Frontiers in physiology. 2014;5:471.
8. Sheldon R, Connolly S, Rose S, Klingenheben T, Krahn A, *et al.* Prevention of Syncope Trial (POST). Circulation. 2006;113(9):1164-70.
9. Totah AR, Benbadis SR. Gelastic syncope mistaken for cataplexy. Sleep medicine. 2002;3(1):77-8.
10. Bloomfield D, Jazrawi S. Shear hilarity leading to laugh syncope in a healthy man. JAMA. 2005;293(23):2859-64.
11. Braga SS, Manni R, Pedretti RFE. "Laughter-induced syncope," Lancet, vol. 366, no. 9483, p. 426, Aug. 2005. [PMID: 16054945 DOI: 10.1016/S0140-6736(05)67027-4]
12. Amaki M, Kamide K, Takiuchi S, Niizuma S, Horio T, *et al.* A case of neurally mediated syncope induced by laughter successfully treated with combination of propranolol and midodrine. International heart journal. 2007;48(1):123-7.
13. Bragg MJ. Fall about laughing: a case of laughter syncope. Emergency Medicine Australasia. 2006;18(5-6):518-9. [PMID: 17083645 DOI: 10.1111/j.1742-6723.2006.00877.x]
14. Lo R, Cohen TJ. Laughter-induced syncope: no laughing matter. The American journal of medicine. 2007;120(11):e5.
15. Famularo G, Corsi FM, Minisola G, De Simone C, Nicotra GC. Cerebellar tumour presenting with pathological laughter and gelastic syncope. European journal of neurology. 2007;14(8):940-3.
16. Nishida K, Hirota SK, Tokeshi J. Laugh syncope as a rare sub-type of the situational syncopes: a case report. Journal of medical case reports. 2008;2(1):197.
17. Awada A, Halaby G, Tamraz J. Spasmodic laughter syncope. An unusual complication of pseudobulbar palsy. Revue neurologique. 2009 Jan;165(1):86-8.
18. Gullapalli DN, Belak ZA, Marte-Grau A, Bollu M, Reddy P, *et al.* Gelastic presyncope: an unusual manifestation in an elderly patient. Journal of the American Geriatrics Society. 2009;57(4):749-50.
19. Shah AA, Gelber AC. Laughter-induced syncope. The American journal of medicine. 2010;123(7):609-11.
20. Thiagarajah PH, Finkielstein D, Granato JE. Sitcom syncope: a case series and literature review of gelastic (laughter-induced) syncope. Postgraduate medicine. 2010;122(6):137-44.
21. Slassi I, El Otmani H, Moutaouakil F, Fadel H. Syncopes gélastiques récurrentes. Rev. Médecine Interne, vol. 33, no. 99, pp. 522–524, 2012. [PMID: 22748313 DOI: 10.1016/j.revmed.2012.06.004]
22. Gaitatzis A, Petzold A. Recurrent Laughter-induced Syncope. The neurologist. 2012;18(4):214-5.
23. Patel SB, Parmar HA, Naik AM. Gelastic syncope: an unusual condition. Natl. Med. J. India, vol. 25, no. 1, p. 21, Feb. 2012. [PMID: 22680316]
24. Haddad C, Haddad-Lacle JE. Laughter-induced syncope. BMJ case reports. 2013 Jul 16;2013:bcr2013010169.

Cite this article : Teuku H,Andri WT, Siswanto BB, Santoso A, Sukmawan R, Sargowo D, Subekti I, Aulanni'am, Siregar NC, Bordosono S. Lowering Inflammation Level by Lp-PLA2 Inhibitor (Darapladib) in Early Atherosclerosis Development: *in vivo* Rat Type 2 Diabetes Mellitus Model. Journal of Cardiovascular Disease Research. 2017;8(3)66-71.