National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Comparative assessment of effects of calcium channel antagonists, amlodipine, and cilnidipine, on QT interval in hypertensive patients - An observational study

Sougata Sarkar, Vartika Srivastava, Manjushree Mohanty

Department of Pharmacology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India

Correspondence to: Vartika Srivastava, E-mail: mscutesmile.1886@gmail.com

Received: September 22, 2017; **Accepted:** November 18, 2017

ABSTRACT

Background: The duration of the QT interval as measured by 12-lead electrocardiography is a measure of myocardial repolarization and is widely used to describe cardiac abnormalities, to determine the presence of cardiac toxicity and to evaluate drug safety. In hypertension, the QT interval is a predictor of the risk of both coronary events and cardiovascular death, after adjusting for the effects of additional risk factors. According to AHA and JNC VIII calcium channel blockers are first-line drug in the treatment of hypertension. The equipotent antihypertensive effect of cilnidipine and amlodipine in their equivalent dose has been demonstrated in number of studies. **Aims and Objectives**: To compare and evaluate the effects of calcium channel antagonists amlodipine and cilnidipine on QT interval among hypertensive patients. **Materials and Methods**: A total of 258 patients were screened, examined, and enrolled as study participants during that period. The enrolled patients were then divided as (1) hypertensive patient (n = 159) - selected patients received either amlodipine (2.5–10 mg) or cilnidipine (5–20 mg) with or without angiotensin receptor blocker (ARB) and (2) hypertensive with controlled diabetic patients (n = 99) - selected patients received either amlodipine (2.5–10 mg) or cilnidipine (5–20 mg) with or without ARB along with antidiabetic medication. Calculated by Bazett's formula (most commonly used) = QT Interval/√ (relative risk [RR] interval) where RR interval = 60/heart rate, normal QTc ≤440 ms. The QT interval was measured at the baseline and after 12 months of treatment for hypertensive patients. **Results**: There was extremely significant QTc reduction was seen with cilnidipine therapy and significant elevation seen by amlodipine treatment but without any clinical relevance. While comparing the effect of amlodipine and cilnidipine, extremely significant as well as clinically relevant difference between the two treatments was noted. **Conclusions**: From this study, it can be concluded that cilnidipine reduces QTc interval, and hence is a better choice over amlodipine for patients suffering from long QT interval.

KEY WORDS: Hypertension; Amlodipine; Cilnidipine; QT Interval

INTRODUCTION

Systemic hypertension is one of the most common non-communicable diseases of humankind affecting about 20% of population globally.[1] All sections of population in India suffer from the disease, with higher prevalence in urban (30.9%) than the rural population (21.2%). Most of the patients with early hypertension have no symptoms, but a regular monitoring of blood pressure attributes to early detection of hypertension.[2] As per 2007 AHA guidelines, calcium channel blockers are one of the first-line drugs in uncomplicated hypertension.[3] According to JNC VIII guidelines, calcium channel blockers are first line of treatment in both general black or non-black population (including those with diabetes).

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.0937418112017	

National Journal of Physiology, Pharmacy and Pharmacology Online 2018. © 2018 Vartika Srivastava, *et al.* This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creative commons.org/licenses/by/4.0/), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

The duration of the QT interval as measured by 12-lead electrocardiography is a measure of myocardial repolarization and is widely used to describe cardiac abnormalities, to determine the presence of cardiac toxicity and to evaluate drug safety. In hypertension, the QT interval is a predictor of the risk of both coronary events and cardiovascular death, after adjusting for the effects of additional risk factors. The mechanism of QT interval prolongation is multifactorial and includes cardiomyocyte hypertrophy and increased left ventricular mass (LVM), with accompanying changes in left ventricular transmural dispersion of repolarization, as well as changes in the tone of the autonomic nervous system of some patients with hypertension and mechanoelectrical feedback, although this mechanism is less likely.

Although blood pressure (BP) reduction is the primary goal of antihypertensive drug therapy and the choice of antihypertensive drug treatment regimens varies among different individuals, the effect of different antihypertensives varies on QTc interval. Hence, the rationale behind this study is to evaluate and compare the effects of two most commonly used CCBs, i.e., amlodipine and cilnidipine on QT interval of hypertensive patients.

Aims and Objectives

To compare and evaluate the effects of calcium channel antagonists Amlodipine and Cilnidipine on QT interval amongst hypertensive patients.

MATERIALS AND METHODS

This is a comparative, non-blinded, single-centered, prospective, and parallel groups; observational study was conducted in medicine outpatient department clinic of Kalinga Institute of Medical Sciences over a period of 24 months. The study was approved by the Institutional Ethical Committee, Kalinga Institute of Medical Sciences, BBSR. Written informed consent of all patients participating in the study was obtained. Hypertensive patients on the basis of inclusion and exclusion criteria were selected for the study.

Inclusion Criteria

- Age: >40 years <60 years; body mass index (BMI) >18.5 <30 kg/m^2 (normal and preobese).
- Sex: Both sexes.
- Patients with essential hypertension of mild-to-moderate cases (Stage I and Stage II) according to JNC 7 (those systolic BP (SBP) <180 and diastolic BP (DBP) <110).
- Phase of microalbuminuria spot urinary albumin-creatinine ratio (ACR), ACR <300 mg/g.
- Hypertensive patients on amlodipine (2.5–10 mg) and cilnidipine (5–20 mg) or combination with angiotensin receptor blocker (ARB) (in a dose equivalent to 40 mg of telmisartan).
- Controlled diabetic patient (hemoglobin A1c [HBA1c] ≤7).

Exclusion Criteria

- Age: <40 years >60 years, BMI <18.5 to >29.99 kg/sq. mt.
- All cases of hypertension with SBP ≥180 and DBP ≥110.
- Patients of secondary hypertension or taking antihypertensive medicine other than additional ACEI/ARB.
- Uncontrolled diabetes (HBA1c >7).
- Serum creatinine ≥1.2.
- Patient with liver disease.
- ACR >300 mg/gm (spot urine).
- Patients on pioglitazone.
- Patients with heart failure, heart block, and aortic stenosis.
- On NSAID for long-term; corticosteroid and sex steroids.
- Any other chronic illness (rheumatoid arthritis, tuberculosis, and protein-energy malnutrition).
- Alcoholic (consume more than moderate amount), hypothyroid, and varicose vein.

Patient Recruitment

Patients with hypertension meeting the above criteria, reporting in the department of medicine between December 14 and November 15 for their treatment, were enrolled in study. A total of 258 patients were screened examined and were selected as study participants during that period. The study was explained to them in local language and written informed consent was obtained. The enrolled patients were then divided as (1) hypertensive patient (n = 159) - selected patients received either amlodipine (2.5–10 mg) or cilnidipine (5–20 mg) with or without ARB, (2) hypertensive with controlled diabetic patients (n = 99) - selected patients received either amlodipine (2.5–10 mg) or cilnidipine (5–20 mg) with or without ARB along with antidiabetic medication.

The QT interval was recorded at the baseline and after 12 months. QTc is corrected QT interval. Calculated by Bazett's formula (most commonly used) = QT interval/√ (relative risk [RR] interval) where RR Interval = 60/heart rate (HR), normal QTc ≤440 ms. A longer QTc puts the patient at increased risk for torsade de pointes.

RESULTS

Table 1 show analysis of QTc (corrected QT interval), on comparison between amlodipine and cilnidipine treatment, on hypertensive (non-diabetic and diabetic) patients. Figure 1 shows comparative analysis of change in QTc with amlodipine and cilnidipine treatment after 12 months. This figure depicts that Amlodipine caused increase in QTc and cilnidipine

caused decrease in QTc. Figure 2 shows comparative analysis of change in QTc with amlodipine and cilnidipine treatment after 12 months. This figure depicts that amlodipine caused increase in QTc and cilnidipine caused decrease in QTc. Scattered diagram in Figure 3 shows extremely significant positive correlation between change in heart rate (HR) and change in QTc (corrected QT interval) with amlodipine treatment in non-diabetic hypertensive patients. Scattered diagram in Figure 4 shows extremely significant positive correlation between change in HR and change in QTc (corrected QT interval) with amlodipine treatment in diabetic hypertensive patients.

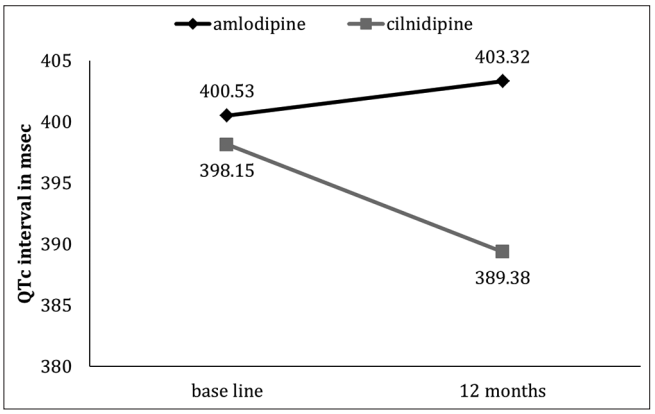

Figure 1: Comparative analysis of change in QTc with amlodipine and cilnidipine treatment after 12 months. This figure depicts that amlodipine caused increase in QTc and cilnidipine caused decrease in QTc

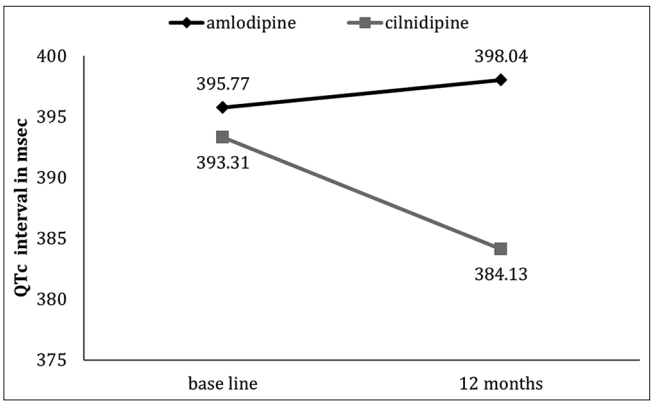

Figure 2: Comparative analysis of change in QTc with amlodipine and cilnidipine treatment after 12 months. This figure depicts that amlodipine caused increase in QTc and cilnidipine caused decrease in QTc

DISCUSSION

In the present study, it was observed that there is statistically extremely significant as well as clinically relevant reduction in QTc interval with cilnidipine treated arm [Table 1, Figures 1 and 2] in both DM (−) ($P < 0.0001$; 95% confident interval (CI); $-10 < -8.77 < -7.45$) and DM (+) ($P < 0.0001$; 95% CI; $-10.58 < -9.17 < -7.76$) patients. On the other hand, amlodipine treated arm [Table 1, Figures 1 and 2] showed statistically extremely significant elevation of QTc in DM (−) ($P < 0.0001$; CI 95%; $1.47 < 2.79 < 4.11$) and in DM (+) ($P = 0.0409$; CI 95%; $0.10 < 2.28 < 4.45$) patients, but this increase in QT interval was not found to be clinically relevant. While comparing the effect of amlodipine and cilnidipine on QTc, it was observed that there was statistically extremely significant and clinically relevant difference between the two treated arms both in non-diabetic ($P < 0.0001$; 95% CI; $8.32 < 13.94 < 19.55$) and diabetic ($P < 0.0001$; 95% CI; $7.26 < 13.91 < 20.56$) patients. In this present study, the total mean change in QTc with the treatment of cilnidipine arm (−8.77 ± 5.87 DM [−] and −9.17 ± 5.06 DM [+]) was much higher than amlodipine treated arm (2.79 ± 5.95 DM [−] and 2.28 ± 7.42 DM [+]). Hence, the change in amlodipine group is very less in this study.

Mozos and Serban concluded that hypertension and LVH are associated with an increased prevalence of prolonged QT intervals.[8] Kang also observed that "although hypertrophy can normalize wall tension, it is a risk factor for QT-prolongation and cardiac sudden death."[9] Klimas *et al.* stated that "progressive increase in duration of QT interval associated with the development of cardiac hypertrophy

Table 1: Analysis of QTc (corrected QT interval), on comparison between amlodipine and cilnidipine treatment, on hypertensive (non-diabetic and diabetic) patients

Data analyzed at mean±SD	Hypertensive patients *n*=159			Hypertensive diabetic patients *n*=99		
	Amlodipine *n*=81	Cilnidipine *n*=78	*P* (95% CI)	Amlodipine *n*=47	Cilnidipine *n*=52	*P* (95% CI)
Base line	400.53±18.96	398.15±18.7	0.4273 NS	395.77±18.37	393.31±16.61	0.4861 NS
12 months**	403.32*±17.93	389.38¥±17.89	0.0001 (8.32<13.94<19.55)	398.04*±19.21	384.13¥±13.94	0.0001 (7.26 <13.91<20.56)
P (95% CI)	0.0001 (1.47<2.79<4.11)	0.0001 (−10<−8.77 < −7.45)		0.0409 (−0.10<2.28 <4.45)	0.0001 (−10.58<−9.17<−7.76)	

SD: Standard deviation, NS: Not significant; CI: Confident interval at 95%. Statics applied. Unpaired *t*-test and paired *t*-test. Predetermined clinically relevant margin is change in 10 ms[4-7] of QTc. Statistically extremely significant ($P<0.0001$) without clinical relevance elevation in QTc seen when compared with baseline. Statistically extremely significant ($P<0.0001$) without clinical relevance decrease in QTc seen when compared with baseline. **Statistically extremely significant ($P<0.0001$) with high clinical relevance difference in QTc seen while comparing amlodipine with cilnidipine treatment

and hypertension not directly related to the increased left ventricular weight which has been documented in spontaneous hypertensive rats."[10] Baumert *et al.* showed that elevated repolarization ability is directly associated with sympathetic cardiac activation in patients with essential hypertension.[11] According to Magnano *et al.*, autonomic conditions directly affect the ventricular myocardium of healthy subjects, causing differences in QT, that are independent of HR.[12] Darbar *et al.* showed that sympathetic activation by a low-salt diet increases sensitivity to drug-induced QT prolongation.[13] It is generally recognized that most, but not all, patients with long QT syndrome (LQTS) experience cardiac events during increased sympathetic activation induced or mimicked by pharmacological agents, physical exercise, stress, or emotion. The role of the ANS in LQTS is furthered by the potential role of the left cardiac sympathectomy in treating these patients.[14-16] According to Klimas *et al.*, antihypertensive drugs vary in their effect on QT interval duration. The mechanisms underlying their effect depend on (a) changes in LVM (b) autonomic nervous system tone, as well as (c) changes in the activity of cardiac ion channels. Although BP reduction is the primary goal of antihypertensive drug therapy and the choice of antihypertensive drug treatment regimens varies among different individuals, the data regarding the disparate effects of antihypertensive drugs on the duration of the QT interval warrant consideration while implementing long-term pharmacotherapy for hypertension. Porthan *et al.* showed "amlodipine seems to have no repolarization effects" which coincides with our study.[17] The study of Milovanović *et al.* showed amlodipine reduces QTc interval (426.94 ± 25.3 vs. 424.08 ± 33.7 ms) without statistical significance,[18] contradict present study (amlodipine elevate QTc, 400.53 ± 18.96 vs. 403.32 ± 17.93 in DM(−); 395.77 ± 18.37 vs. 398.04 ± 19.21 in DM(+) patients). Ashizawa *et al.* showed prolonged QT interval was shortened (from 441.9 ± 25.2 to 427.6 ± 29.8, $P < 0.05$) by cilnidipine in hypertensive patients through attenuation of sympathetic activity,[19] and QTc interval shortening was correlated with HR reduction ($r = 0.3184$, $P = 0.04$) in their study that partially contradict our study. The present study showed no correlation between total mean change of HR and QTc in the cilnidipine treated arm, on the other hand, amlodipine treated arm showed highly positive correlation ($r = 0.942$; $r^2 = 0.89$; $P < 0.0001$ in DM(−) and $r = 0.945$; $r^2 = 0.89$; $P < 0.0001$ in DM(+) patients) [Figures 3 and 4]. It is an indication that there may another mechanism by which cilnidipine reduces QTc. In a previous study by Takahara *et al.* demonstrated that ventricular repolarization process was little affected by acutely administered cilnidipine in this animal model, indicating that it cannot be simply explained by its immediate effects on sympathetic N-type and vascular L-type Ca^{2+} channels, goes with our results.[20]

The mechanism of QT interval prolongation is multifactorial and includes cardiomyocyte hypertrophy and increased LVM, with accompanying changes in the left ventricular

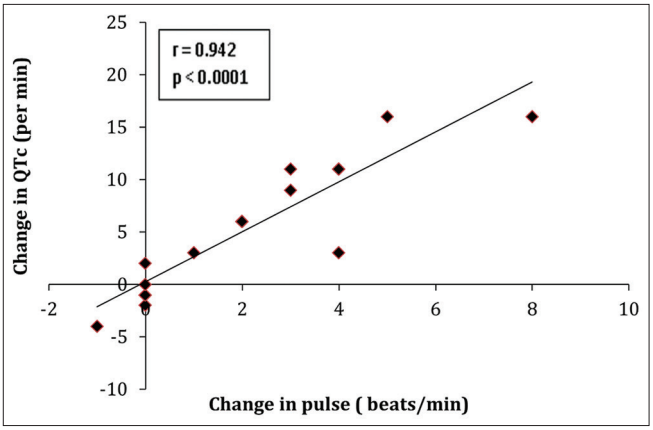

Figure 3: Scattered diagram shows extremely significant positive correlation between change in heart rate and change in QTc (corrected QT interval) with amlodipine treatment in non-diabetic hypertensive patients

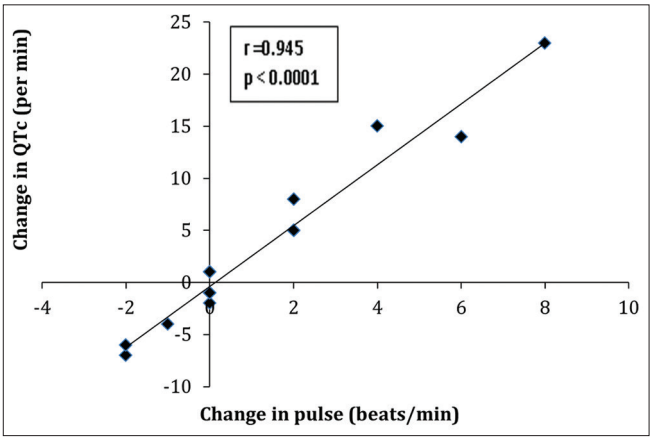

Figure 4: Scattered diagram shows extremely significant positive correlation between change in heart rate and change in QTc (corrected QT interval) with amlodipine treatment in diabetic hypertensive patients

transmural dispersion of repolarization, as well as changes in the tone of the autonomic nervous system of some patients with hypertension and mechanoelectrical feedback, although this mechanism is less likely. A few studies have already demonstrated that LVH results in prolonged and non-uniform ventricular repolarization, increased action potential duration, and delayed ventricular conduction.[21-23] The prolonged QT interval may be attributed to the increased thickness of the left ventricle wall and to intramural fibrosis, which distorts and prolongs transmural impulse propagation which may be a manifestation of the intraventricular or interventricular conduction delay or block, or it may be due to the downregulation of several potassium currents responsible for repolarization.[24,25] Study of Takahara *et al.* concluded that the QT interval and monophasic action potential durations were shortened only in the cilnidipine group, but such effects were not observed in the amlodipine group, using heart of canine chronic atrioventricular block model[26] (cardiac sudden death model) is known to have a ventricular electrical remodeling, which mimics the pathophysiology of LQTS.

The effect of cilnidipine on QTc depression is more than amlodipine and was clearly analyzed in the present study. The cellular mechanism(s) by which cilnidipine shortens the ventricular repolarization has not been fully elucidated at present. Previous *in vitro* electrophysiological studies have demonstrated that angiotensin II decreases IKr, transient outward K+ currents (Ito) and inward rectifier K+ currents (IK1) of the cardiomyocytes[27-29] and that aldosterone decreases Ito.[30] Based on the differences in the effects on the neurohumoral factors between cilnidipine and other drugs, it can be speculate that the inhibitory effect of cilnidipine on the renin-angiotensin-aldosterone system by its N-type calcium channel blocking action[31-34] may have decreased the suppression of the K+ channels. It is well known that angiotensin II and aldosterone have direct proarrhythmic effects which by several BP-independent mechanisms such as an increase in sympathetic activation, increases in extracellular Ca^{2+}entry and Ca^{2+} release from intracellular stores and modulation of voltage-dependent potassium channels stated above.

Hence, the present study throws some light on the availability of better CCB in hypertensive patients with prolong QT interval as because QT interval is a predictor of the risk of both coronary events and cardiovascular death, after adjusting for the effects of additional risk factors. As this study was done just for 24 months, much bigger studies are required with more number of participants for better clinical implications. Furthermore, other antihypertensive group of drugs like ACE inhibitors should be analyzed for similar effect.

CONCLUSIONS

From this study, it can be concluded that cilnidipine reduces QTc interval and hence is a better choice over amlodipine for patients suffering from long QT interval.

ACKNOWLEDGMENTS

As it is a collaborative work with department of medicine, we would like to thank all staff members of medicine and pharmacology department for their immense support.

REFERENCES

1. Krishnadas KV. Text Book of Medicine. 4th ed., Vol 2. New Delhi: Jaypee Brothers; 2004. p. 651.
2. Rung MS, Greganti AM. Netter's Internal Medicine. USA: Icon Learning Systems LLC; 2003. p. 127-8.
3. Saseen JJ. Hypertension, applied therapeutics In: Koda-Kimble MA, Young LY, Alldredge BK, editors. The Clinical use of Drugs. 9th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2009. p. 13-8.
4. Ayad RF, Assar MD, Simpson L, Garner JB, Schussler JM. Causes and management of drug-induced long QT syndrome. Proceedings (Bayl Univ Med Cent) 2010;23:250-5.
5. Drew BZ, Ackerman MJ, Funk M, Gibler WB, Kligfield P, Menon V, *et al.* Prevention of torsade de pointes in hospital settings. J Am Coll Cardiol 2010;55:934-47.
6. Moss AJ, Schwartz PJ, Crampton RS, Tzivoni D, Locati EH, MacCluer J, *et al.* The long QT syndrome. Prospective longitudinal study of 328 families. Circulation 1991;84:1136-44.
7. Zareba W, Moss AJ, Schwartz PJ, Vincent GM, Robinson JL, Priori SG, *et al.* Influence of the genotype on the clinical course of the long-QT syndrome. International long-QT syndrome registry research group. N Engl J Med 1998;339:960-5.
8. Mozos I, Serban C. The relation between QT interval and T-wave variables in hypertensive patients. J Pharm Bioallied Sci 2011;3:339-44.
9. Kang YJ. Cardiac hypertrophy: A risk factor for QT-prolongation and cardiac sudden death. Toxicol Pathol 2006;34:58-66.
10. Klimas J, Vaja V, Vercinska M, Kyselovic J, Krenek P. Discrepant regulation of QT (QTc) interval duration by calcium channel blockade and angiotensin converting enzyme inhibition in experimental hypertension. Basic Clin Pharmacol Toxicol 2012;111:279-88.
11. Baumert M, Schlaich MP, Nalivaiko E, Lambert E, Sari CI, Kaye DM, *et al.* Relation between QT interval variability and cardiac sympathetic activity in hypertension. Am J Physiol Heart Circ Physiol 2011;300:H1412-7.
12. Magnano AR, Holleran S, Ramakrishnan R, Reiffel JA, Bloomfield DM. Autonomic nervous system influences on QT interval in normal subjects. J Am Coll Cardiol 2002;39:1820-6.
13. Darbar D, Fromm MF, Dellorto S, Roden DM. Sympathetic activation enhances QT prolongation by quinidine. J Cardiovasc Electrophysiol 2001;12:9-14.
14. Antzelevitch C, Shimizu W. Cellular mechanisms underlying the long QT syndrome. Curr Opin Cardiol 2002;17:43-51.
15. Noda T, Takaki H, Kurita T, Suyama K, Nagaya N, Taguchi A, *et al.* Gene-specific response of dynamic ventricular repolarization to sympathetic stimulation in LQT1, LQT2 and LQT3 forms of congenital long QT syndrome. Eur Heart J 2002;23:975-83.
16. Schwartz PJ, Priori SG, Cerrone M, Spazzolini C, Odero A, Napolitano C, *et al.* Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. Circulation 2004;109:1826-33.
17. Porthan K, Viitasalo M, Hiltunen TP, Vaananen H, Dabek J, Suonsyrja T, *et al.* Short-term electrophysiological effects of losartan, bisoprolol, amlodipine, and hydrochlorothiazide in hypertensive men. Ann Med 2009;41:29-37.
18. Milovanović B, Trifunović D, Milićević N, Vasić K, Krotin M. The significance of amlodipine on autonomic nervous system adjustment (ANSA method): A new approach in the treatment of hypertension. Srp Arh Celok Lek 2009;137:371-8.
19. Ashizawa N, Seto S, Kitano K, Toyama K, Sasaki H, Kodama K, *et al.* Effects of blood pressure changes on development and regression of electrocardiographic left ventricular hypertrophy: A 26 year longitudinal study. J Am Coll Cardiol 1989;13:165-72.
20. Takahara A, Sugiyama A, Satoh Y, Nakamura Y, Hashimoto K. Cardiovascular effects of an L/N-type ca2+ channel blocker cilnidipine assessed in the chronic atrioventricular conduction block dogs. J Pharmacol Sci 2004;96:219-23.
21. Zhao Z, Yuan Z, Ji Y, Wu Y, Qi Y. Left ventricular hypertrophy

amplifies the QT, and Tp-e intervals and the Tp-e/QT ratio of left chest ECG. J Biomed Res 2010;24:69-72.
22. Mozos I, Costea C. The QT interval and left ventricular hypertrophy in essential hypertension. In: Sobieszczanska M, Jagielski J, Macfarlane PW, editors. Electrocardiology. Proceedings of the 36th International Congress on Electro Cardiology. Wroclaw, Poland: JAKS Publishing Company; 2010. p. 203-9.
23. Oikarinen L, Nieminen MS, Viitasalo M, Toivonen L, Jern S, Dahlöf B, *et al.* QRS duration and QT interval predict mortality in hypertensive patients with left ventricular hypertrophy: The losartan intervention for endpoint reduction in hypertension study. Hypertension 2004;43:1029-34.
24. Hancock EW, Deal BJ, Mirvis DM, Okin P, Kligfield P, Gettes LS. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: Part V: Electrocardiogram changes associated with cardiac chamber hypertrophy. Circulation 2009;19:e251-61.
25. Xu X, Rials SJ, Wu Y, Salata JJ, Liu T, Bharucha DB, *et al.* Left ventricular hypertrophy decreases slowly but not rapidly activating delayed rectifier potassium currents of epicardial and endocardial myocytes in rabbits. Circulation 2001;103:1585-90.
26. Takahara A, Nakamura Y, Wagatsuma H, Aritomi S, Nakayama A, Satoh Y, *et al.* Long-term blockade of L/N-type ca (2+) channels by cilnidipine ameliorates repolarization abnormality of the canine hypertrophied heart. Br J Pharmacol 2009;158:1366-74.
27. Yu H, Gao J, Wang H, Wymore R, Steinberg S, McKinnon D, *et al.* Effects of the renin-angiotensin system on the current Ito in epicardial and endocardial ventricular myocytes from the canine heart. Circ Res 2000;86:1062-8.
28. Domenighetti AA, Boixel C, Cefai D, Abriel H, Pedrazzini T. Chronic angiotensin II stimulation in the heart produces an acquired long QT syndrome associated with IK1 potassium current down regulation. J Mol Cell Cardiol 2007;42:63-70.
29. Wang YH, Shi CX, Dong F, Sheng JW, Xu YF. Inhibition of the rapid component of the delayed rectifier potassium current in ventricular myocytes by angiotensin II via the AT1 receptor. Br J Pharmacol 2008;154:429-39.
30. Bénitah JP, Perrier E, Gómez AM, Vassort G. Effects of aldosterone on transient outward K+ current density in rat ventricular myocytes. J Physiol 2001;537:151-60.
31. Takemori K, Ishida H, Dote K, Yamamoto K, Ito H. Prophylactic effects of an N-and L-type ca2+ antagonist, cilnidipine, against cardiac hypertrophy and dysfunction in stroke-prone, spontaneously hypertensive rats. Can J Physiol Pharmacol 2005;83:785-90.
32. Konda T, Enomoto A, Takahara A, Yamamoto H. Effects of L/N-type calcium channel antagonist, cilnidipine on progressive renal injuries in Dahl salt-sensitive rats. Biol Pharm Bull 2006;29:933-7.
33. Konda T, Enomoto A, Aritomi S, Niinuma K, Koganei H, Ogawa T, *et al.* Different effects of L/N-type and L-type calcium channel blockers on the renin-angiotensin-aldosterone system in SHR/Izm. Am J Nephrol 2009;30:155-61.
34. Aritomi S, Nogi Y, Koganei H, Mitsui A, Konda T, Yoshimura M. The role of N-type calcium channels in regulating aldosterone secretion in H295R human adrenocortical cells. J Am Soc Nephrol 2007;18:155A.

How to cite this article: Sarkar S, Srivastava V, Mohanty M. Comparative assessment of effects of calcium channel antagonists, amlodipine, and cilnidipine, on QT interval in hypertensive patients - An observational study. Natl J Physiol Pharm Pharmacol 2018;8(4):530-535.

Source of Support: Nil, **Conflict of Interest:** None declared.