Research Article

Ivabradine: A Novel Drug to Control Heart of Patients Undergoing CT Coronary Angiography

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Abstract: Heart rate control is crucial for diagnostic accuracy and proper image quality of CTCA. A lower heart rate reduces coronary artery movement artifacts by increasing the length of diastolic phase, thereby improving image quality as blood stay longer in vessels. Despite wide spread use of β-blockers ,it has been difficult to achieve target heart rates in patients undergoing CTCA. Ivabradine is a novel purely negative chronotropic drug which acts on sinus node &decreases heart rate without significant hemodynamic effects or impairment of cardiac conduction. Our study assessed the efficacy of ivabradine on image quality of CT coronary angiography (CTCA) and compared it with β- blockers. We randomized 100 consecutive patients undergoing CTCA to receive either of the two premedication protocols: oral β-blockers or ivabradine. Images were scored in terms of image quality of the coronary artery segments using a 5-point grading scale. Ivabradine achieved better heart rate reduction & also required less additional pre study doses of rate controlling drugs. CTCA image quality with ivabradine group had 95% diagnostically accepted coronary segments imaging compared to 90% with the β – blocker group. β- blocker significantly lowered both systolic and diastolic blood pressure, while ivabradine did not. Ivabradine is an attractive alternate to β- blocker for reduction of heart rate in patients undergoing CTCA and had an excellent safety profile.

Keywords: Ivabradine, 64-slice Computed Tomography Coronary Angiography, Heart rate control,β- blocker, Image quality: CTCA, low side effect, CAD.

INTRODUCTION

The rapid technological development of computed tomography coronary angiography (CTCA) over the past decade has significantly increased our ability to image the heart and coronary arteries noninvasively. Essential to performing a successful CTCA examination is obtaining proper image quality without motion artefacts, which depends on a low and stable heart rate. Despite significant technical advances, heart rate control remains an important factor in optimizing the image quality of CTCA[1]. To achieve heart rate reduction, β-blocking medication has been routinely administered prior to CTCA examinations. The use of β-blockers is however limited due to contraindications& side effects. In recent studies, a substantial portion of patients requiring heart rate reduction had contraindications to β-blockers [1,2].

Ivabradine is a novel & promising heart-rate lowering anti anginalagent, that reduces the heart's natural pacemaker (sinus node) activity by inhibiting the If (funny) ion channels[3]. Moreover, ivabradine inhibits the Ifcurrent at concentrations that do not affect other cardiac ionic currents, resulting in a lack of hemodynamic effects such as reduction of blood pressure or cardiac contractility, which is often a limitation with β-blockers. It has a good safety profile without any effects on atrio-ventricular conduction, corrected QT interval and peripheral vasomotion and there is no rebound effect with drug cessation or tolerance with prolonged use[4].

Since this drug has minimal hemodynamic effects, lower side effects & is very well tolerated it is a very attractive alternate to β-blockers. Therefore, this study was conducted to evaluate the efficacy of Ivabradine for heart rate control in patients undergoing 64slice CT Coronary angiography and to compare it with β-blockers.

Aims and Objectives

To assess the effectiveness of ivabradine on heart rate reduction and thereby improving image quality of ECG-gated multi detector CT (MDCT) coronary angiography & to compare it with β–blockers as premedication.

MATERIALSANDMETHODS

This prospective study was carried out in Department of Radio diagnosis& Cardiology, Sri Aurobindo Medical College and P.G. Institute, Indore from May 2012 to October 2013 over period of eighteen months with approval from institutional research and ethical committee. A total of 100 consecutive patients referred for CTCA for the evaluation of suspected coronary artery disease (CAD) were enrolled in the study. After obtaining informed consent, patients were randomized to receive either of the two premedication protocols: oral β-blockersor oralivabradine at the prescribed doses for 24 to 48 hours prior to the study.

The patients achieving target heart rate ≤65 beats per minute (bpm) were subjected to CTCA by using standard institutional protocol. Axial source, multiplanar reconstruction, maximum intensity projection, and volume-rendered images were used for assessment of the coronary arteries. Image quality was assessed by two radiologists who independently reviewed the images; eight of 15 coronary segments differentiated according to the "American Heart Association classification":

- Left Main Coronary Artery (LMCA);
- Proximal and Middle Segments of the Left Anterior Descending (LAD)
- Proximal and Middle segments of Left Circumflex (LCX)
- Proximal, Middle, and Distal Segments of the Right Coronary Artery (RCA).

A 5-point scale was used to assess the image quality of each coronary segment:

- 5 - no motionartifacts;
- 4 - minor artifacts (mild blurring);
- 3 - moderate artifacts (moderate blurring without discontinuity);
- 2 - severe artifacts (doubling or discontinuity in the course of the coronary segments);
- 1 - unreadable (vessel structures not differentiable)

Score of 4 or higher was considered acceptable image quality. The number of patients with acceptable image quality in each coronary segment was calculated and the results were compared between the two groups.

OBSERVATIONS

Table 1: Percentage of patients achieving target heart rate (<65 bpm) before undergoing CTCA

	Group I Ivabradine(bpm)	Group II β- Blocker(bpm)
Day of Appointment	75±7	77±10
Day of CTCA	66±5	73±8
During CTCA	60±4	65±7
Total reduction of heart rate	15±7	12±8.5
% of reduction of heart rate from base line	20%	15.58%

Our study revealed that heart rate was better controlled by ivabradine in comparison to β – blocker drugs.

Table 2: Percentages of patients with acceptable image quality in coronary segments

Artery	LMCA	LAD		LCX		RCA		
Group		Proximal	Middle	Proximal	Middle	Proximal	Middle	Distal
Ivabradine	100%	100%	100%	94%	96%	96%	89%	96%
β–blocker	96%	97%	93%	92%	91%	91%	82%	92%

Our study revealed better acceptable image quality in coronary segments in Ivabradine group.
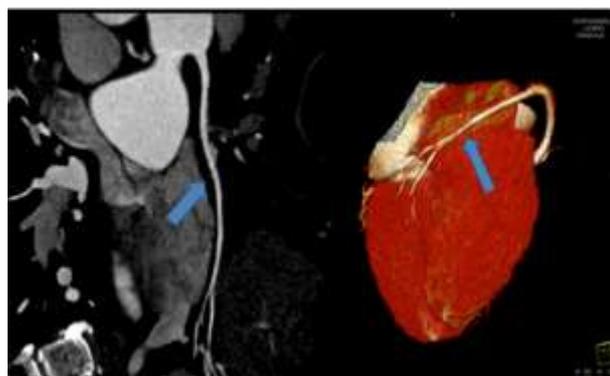
Fig.1:No motion artifacts (RCA): Score of 5 Points

Fig. 2: Minor artifacts (Middle segment of LCx):Score of 4 Points
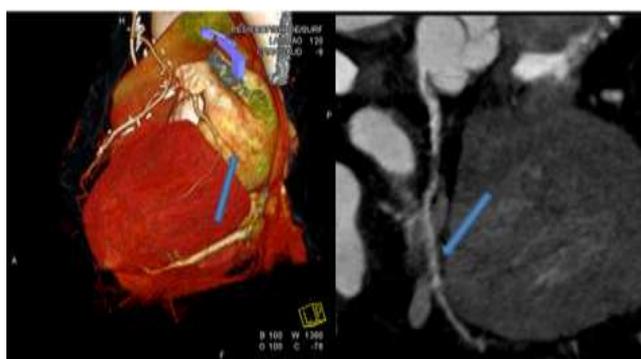

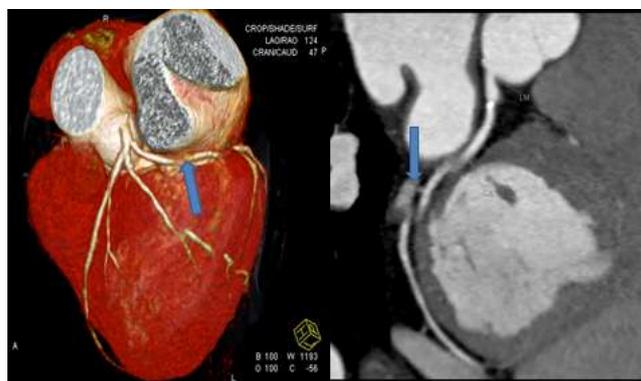**Fig. 3: Moderate artifacts (Proximal and Distal segments of LCx): Score of 3 Points**

Fig. 4: Severe artifacts (discontinuity in Proximal segment of LCx):Score OF 2 Points

RESULTS

In our study, we had taken total consecutive 100 patients, out of these 58(58%) patients, who received oral ivabradine, kept in group I. While 42(42%) patient, who receivedβ- blocker kept, in group II. The heart rate was recorded before giving medicine and during CTCA. Majority of the patients in our study were in age 56 to 60 with male predominance. In our study, ivabradine group showed reduction in heart rate of 15+7, while with β-blocker the reduction in heart rate were only 12+ 8.5bpm. So during CTCA, mean heart rate were 60+4 and 65+7 with group I and II respectively. Our study revealed acceptability of image quality of LMCA was 100% in ivabradine group, while 96% patient with β-blocker group. In proximal part of RCA and middle part of LCX, acceptability of image quality was 96% and 91% with group I and II respectively.

DISCUSSION

CTCA has emerged as an excellent non-invasive tool for the diagnosis of CAD [5–7]. However, adequate image quality is essential to achieve optimal diagnostic accuracy, and having a heart rate of 60–65bpm during imaging has been strongly recommended for this. An essential part of performing a successful CTCA examination has been tooptimize the patient's heart rate using β-blockers to limit motion artifacts in the coronary arteries. However, despite the routine use of β-blockers prior to CTCA studies, it is not uncommon to have patients with heart rates persistently

above the target range of 65 bpm, despite using oral as well as intra venous b-blockers [8–10].

Ivabradine is a novel heart rate-lowering agent that selectively inhibits the If current, which primarily contributes to sinus node pacemaker activity, without affecting other cardiac ionic currents [11–13]. Hence, there are no significant direct cardiovascular effects such as reduction of blood pressure, cardiac contractility or impairment of cardiac conduction. In fact, in contrast to b-blockers, If current inhibition increases stroke volume and may improve left ventricular function and ventricular remodeling [14]. The safety and efficacy of ivabradine in chronic stable angina and in patients with CAD with impaired left ventricular (LV) function, as monotherapy as well as add-on therapy to β-blockers, has been well demonstrated [15–17]. Ivabradine has been noted to be particularly beneficial in patients with high resting heart rates, a property that can be especially useful in patients undergoing CTCA. Side effects are infrequent and mostly restricted to dose related visual disturbances, which are however rare if doses are kept to less than 10mg BD[15, 18] and unlikely to be seen with the short time use for CTCA.

Majority of the patients in our study were in age 56 to 60 with male predominance. Target heart rate was achieved better with ivabradine and also number of patients requiring additional doses of drugs prior to study was significantly less in group ivabradine. In our study, the reduction in heart rate was 15 ± 7, while with β- blocker the reduction in heart rate was only 12 ± 8.5. The percentage of total reduction of heart rate from base line was 20 % and 15.58% with group I and II receptively. Our results were equivalent to Naiyanel*et al.* [19] which showed the mean absolute reduction of heart rate of 15.04 ± 8.03 bpm. The heart rate decreased approximately 20% from the base line with ivabradine group. A lower heart rate reduces coronary artery movement artifact by increasing the length of diastolic phase thereby increasing CTCA image quality because blood stay little longer in vessels [20].

In our study, Image quality of LMCA and LAD was found to be 100 and 96% which was equivalent to Ümmügülsüm Bayraktutan *et al.*[20], while Image quality of middle portion of RCA and the LCX artery was lower than the other segments (aprox 96 and 91% in group I &II respectively) due to their close to the right and left atria respectively, As lu B & Mao SS et al study mentioned that RCA and the LCX artery are more prone to motion artifacts, due to close proximity to the right and left atria, respectively [21].CTCA image quality in the group treated with Ivabradine premedication performed 95% diagnostically accepted coronary segments compared to 90% with β – blocker premedication, which was equivalent toÜmmügülsüm Bayraktutan *et al.* [20] their results revealed 95.5% diagnostically acceptable coronary segments in ivabradine group compared to 89.8% with beta blocker premedication.

CONCLUSION

CTCA with oral ivabradine premedication is a feasible, safer and more effective way of reducing heart rate to generate image of diagnostically acceptable quality in almost all coronary segments in comparison to β- blockers. Ivabradine can also be successfully used in patients with contraindications to β- blockers.

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