Pak Heart J

THE EFFECT OF METOPROLOL ALONE AND METOPROLOL PLUS BROMAZEPAM ON HEART RATE AND HEART RATE VARIABILITY DURING MULTISLICE COMPUTED TOMOGRAPHY ANGIOGRAPHY

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Date Received: February 03, 2012
Date Revised: March 09, 2012
Date Accepted: March 17, 2012

Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

All authors declare no conflict of interest.

ABSTRACT

Objective: The purpose of this study was to determine the effect of metoprolol alone and metoprolol plus bromazepam on heart rate and heart rate variability during multi slice computed tomography (MSCT) angiography.

Methodology: This was a Double blind randomized controlled trial was conducted at AFIC/NIHD, Rawalpindi, from May 2011 to November 2011. Patients undergoing first MSCT angiography meeting inclusion criteria with heart rates (HR) more than 80 beats/min were included. Patients were randomized in to two groups using random numbers table. Group 1 was administered metoprolol plus placebo while group 2 was administered metoprolol plus bromazepam one hour before the scan. Both groups had scans under strictly similar conditions. HR before and during scan along with heart rate variability (HRV) were recorded.

Results: A total of 80 patients were included. Patients mean age was 49 $\pm$ 13, 57 % were males while 43 % were females. Risk factor profile was similar in both groups. HR reduction in group 1 was 15$\pm$ 6.0 and in group 2, was 21$\pm$9.0 (p= 0.002). HRV in group 1 was 3.9$\pm$ 1.32 and in group 2 was 2.3$\pm$1.0 (p= 0.003). Group 2 had significantly lower HR and significantly less HRV as compared with group 1.

Conclusion: Combination of bromazepam and metoprolol results in significant and further reduction in heart rate and heart rate variability than metoprolol alone. Both drugs can be used together for a better control of heart rate and heart rate variability during MSCT angiography for improving the quality of images.

Key Words: Metoprolol, Bromazepam, Heart rate (HR), Heart rate variability(HRV), Multi Slice Computed Tomography (MSCT) angiography.

INTRODUCTION

Multi Slice Computed Tomography (MSCT) angiography has established itself as an alternative first line test which is noninvasive as well as less expensive to rule out coronary artery disease.[1,2,3] Earlier generation scanners had lower temporal resolution and as a result the scans lacked clarity and thus accurate diagnosis of coronary artery disease was not possible. Several previous studies using 16- and 64-slice computed tomography have demonstrated an inverse relationship between heart rate and image quality concerning coronary artery visualization and detection of stenosis.[4,5] After adequate patient preparation (which includes lowering of the heart rate), rates of sensitivity ranging from 83% to 99% and specificity between 93% and 98% have been reported for the detection of coronary artery stenosis in comparison with invasive coronary angiography.[1]

Newer generation scanners like Dual Source Computed Tomography (DSCT) scanners use two tubes and have temporal resolution of 83 milliseconds and excellent quality scans are obtainable.[6] However, image quality still remains somewhat dependent on heart rate.[7] Currently most authors recommend lowering the patient's heart rate to <65 beats/min to achieve best image quality.[8-11] Although with DSCT scanners good scans can be obtained at heart rate as high as 90 beat/min but best scans are still obtained at heart rates of 60-70 beat/min. In 100 patients studied without beta-blocker pre-medication, DSCT demonstrated slightly lower per-segment evaluability for high heart rates. [12] Modern scanners set the parameters of acquisition automatically.

Current ECG-pulsing algorithms are able to detect ectopic heart beats and the x-ray tube current modulation is automatically switched off until the heart rate is stable again, however, sudden changes in heart rate can lead to low quality scans.[13] Optimal ECG pulsing, compared with a fixed ECG pulsing window at 25%–70% of the R-R interval, can help to reduce the effective radiation dose by 64% in patients with low heart rates.[14] Beta blockers are almost routinely used to control heart rate and metoprolol is the most commonly used beta blocker followed by atenolol.[7] Beta blockers reduce heart rate and blood pressure, have a calming effect on the patient, but still many patients have sudden jump in the heart rate due to natural anxiety during the scan.

Bromazepam is an effective anxiolytic from benzodiazepine group with somatic as well as global effects and has been successfully used as premedication.[15,16] We proposed that addition of an anxiolytic will lead to further reduction in heart rate and prevent anxiety related changes in the heart rate also called heart rate variability (HRV) during the scan. This would ultimately lead to better quality scans (less artifacts) along with reduction of radiation dose to the patient.

The purpose of this study was to determine the effect of Metoprolol alone and Metoprolol plus Bromazepam on heart rate and heart rate variability during multi slice computed tomography angiography.

METHODOLOGY

The randomized double blind controlled trial was conducted at Cardiac Scan Department AFIC/NIHD, Rawalphindi, from May 2011 to November 2011. Data was collected through a history & procedure details Performa. All patients with heart rates more than 80 beats/min while at rest and age between 25 to 65 years under going first MSCT scan for the probable diagnosis of coronary artery disease were included in the study. Both male and females were included. Patients with prior history of CABG, PTCA/Stenting, with contraindications to beta blockers, with arrhythmia, allergy to iodinated contrast, already using beta blockers, anxiolytics, sedative and hypnotics, and known cases of ischemic heart disease (IHD) and those patients who already had a MSCT scan were excluded. Patients who underwent scans in emergency were excluded. All patients gave written informed consent.

A sample of 80 patients was planned using non-probability convenience sampling and randomly divided into two groups after initial selection using random number table. Group 1 was administered tablet metoprolol 100mg ½ tablet (tab Mepressor by Novartis®) plus a placebo and group 2 was administered tablet Mepressor 100 mg ½ tablet plus tablet bromazepam 3mg (tab Lexotanil 3 mg by Roche®) one hour before scan.

The variables for this study included heart rate of the patients before the test and heart rate during the test and heart rate variability during the test. Heart rates were recorded by a doctor for one complete minute just before the test while patients were still in the waiting room and during the test while on the scanning table just after the Calcium scoring. All scans were performed on Somatom Definition DSCT scanner from Siemens using same scan protocols and nonionic iodinated contrast agent Iopromide (Ultravist-370 by Bayer schering pharma).

Patients were blinded to the medications; similarly doctor recording the heart rate was blinded to the identity of patient groups. Data of the sample study was of quantitative nature and sample size was enough to make distribution normal. To exclude other factors contributing to heart rate changes, consenting doctor, paramedic administering the medication and doctors recording the heart rate were the same for all patients and similarly technicians carrying out the scans, auditory instructions and doctors supervising the scan were also the same. All Patients waited for at least one hour (range 1-3hours) in the waiting area of cardiac scan department. All

scans were carried out by appointment and done in the morning time before noon and as outdoor procedures.HRV was defined as the standard deviation of the mean heart rate during CT coronary angiography.

Data Analysis was done by using SPSS (version 16.0). Frequencies and percentages were shown for qualitative variables. Mean and standard deviation (SD) were used for quantitative variables. Chi square test was applied to qualitative variables while independent samples t-test was used for quantitative variables between both the groups. P-value < 0.05 was considered as significant.

RESULTS

A total of 80 patients were included. Table 1 illustrates patient baseline characteristics. Table 2 shows risk factor profile of the two groups. Hypertension was most prevalent among risk factors followed by smoking history and diabetes mellitus.

Table 3 shows that the use of two drugs (i.e. metoprolol and bromazepam) in combination significantly lowered the heart rate variability and significantly lowered the heart rate as well with reduction of 21 ± 9.0 beats/min.

DISCUSSION

The patient groups consisted of a well-defined patient population referred for their first diagnostic MSCT angiogram with the diagnosis of probable coronary artery disease. Risk factor profile was similar to reported earlier.[17] Peak effect of both metoprolol and bromazepam is achieved after an hour. Metoprolol 50 mg administered orally 1 hour before scanning has been reported to be effective, especially in patients without history of prior use of the medication.[18] Both

Table 1: Patient Baseline Characteristics

Characteristic	Total Patients (n=80)	Group 1 (Metoprolol + Placebo) n =40	Group 2 (Metoprolol + Bromzepam) n=40	P-value
Age (years)	49 ± 13	50.49 ±14.66	48.42 ± 11.47	0.499
Gender				
Male	46 (57 %)	27 (34%)	19 (24%)	0.070
Female	34 (43 %)	13 (16%)	21 (26%)	

Table 2: Risk Factor Profile

Risk factor	Group 1 n(%)	Group 2 n(%)	P-value
Hypertension	8(20%)	9(22.5)	0.784
Smoking	7(17.5%)	8(20%)	0.774
Diabetes Mellitus	5(12.5%)	4(10%)	0.723
Hyperlipidemia	4(10%)	5(12.5%)	0.723
Family History of IHD	6(15%)	4(10%)	0.498

Table 3: Reduction in Heart Rate and Heart Rate Variability by Medication Group

Variables	Group 1	Group 2	P-value
Heart Rate Variability	3.9 ± 1.32	2.3±1.0	0.003
Reduction in Heart Rate (beats/min)	15 ± 6.0	21 ± 9.0	0.002

treatment groups showed significant drop in the heart rate but the magnitude of drop was much bigger and statistically significant, in case of group 2.

Anxiety about the test itself and worry about consequences of an abnormal report can cause tachycardia. Beta blockers control somatic effects of but do not control anxiety itself and when used in combination addition of an anxiolytic treats not only anxiety but also its somatic effects. Reducing average heart rate and heart rate variability both are beneficial for reduction of artifacts.[19] Heart rate variability was also less in the group 2. Again anxiolytics may reduce the effects of visiting the scan room for the first time, movement in the scan machine and nervousness to obey the breath holding commands and finally feeling of warmth due to contrast rushing through.

On a per-patient, per-vessel, and per-segment basis, DSCT angiography has a high sensitivity and specificity for the diagnosis of coronary artery stenosis but HRV and calcium score still have a statistically significant effect on the sensitivity and specificity of DSCT angiography.[20] Although adaptive ECG pulsing is now robust and generally effective, however, it should be noted that the dose reduction feature of ECG pulsing is almost completely eliminated in patients with severe HRV because it is partly or totally switched off throughout the examination in patients with arrhythmia to maintain diagnostic image quality.[13]

Recently, sequential or step-and-shoot computed tomography (CT) coronary angiography has gained renewed interest as a technique to reduce radiation exposure while preserving diagnostic image quality. However, step-and-shoot CT coronary angiography is currently limited to selected patients with low and regular heart rates only.[21-23]

Use of beta-blockers in combination with anxiolytics like bromazepam may help achieve slower and stable heart rates thus making possible use of step and shoot mode for MSCT angiography. Beta blockers are also used to reduce and stabilize heart rate in patients undergoing cardiac scans with atrial fibrillation.[24]

Future developments leading to complete acquisition during a single heart beat with a further increase in temporal resolution may result in a true heart rate-independent image acquisition thus obviating the need of premedication. But at present it is recommended that a combination of beta blockers and anxiolytics may be used to obtain lower and stable heart rates for best quality scans with minimum heart rate related artifacts.

CONCLUSION

Combination of metoprolol and bromazepam results in significant and further reduction in heart rate and heart rate variability than metoprolol alone. Both drugs can be used in combination to achieve a better control of heart rate and heart rate variability during MSCT angiography.

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