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Overconsumption of Contrast Media in Percutaneous Coronary Intervention: Focusing on Cost and Acute Kidney Injury

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Abstract

Irrational use of medicines is a major problem worldwide. Since iodixanol (Visipaque®) was categorized in Category I based on the ABC-VED analysis in our hospital, we evaluated the amount of visipaque use and estimated the incremental cost based on the Maximum Contrast Dose (MCD) following irrational use of contrast media.

This retrospective study was conducted on 100 admitted patients aged 18 to 80 years old undergoing elective Percutaneous Coronary Intervention (PCI) who received visipaque during February 2016 to January 2017. All of the patients' information was collected from medical records and Hospital Information System (HIS). MCD was calculated by using the formula proposed by Cigarroa and colleagues: MCD (mL) =5× body weight (kg)/ Serum Creatinine (SCr) (mg/dl). The amount of contrast media administered ranged from 200 to 600 mL (mean, 348 mL ± 80). 57 % of patients received the visipaque more than MCD. Only 25 patients were evaluated SCr after PCI and in 11 (44%) of these patients SCr increased and 3 (12%) patients developed CI-AKI. Consumption of the contrast media was 2 to 3 times more than previous studies which could be the cause of acute kidney injury besides the extra cost. In our study about six liters more of contrast agent was used which is more than standard values with a cost of approximately $2,000 for 100 patients. Therefore, in order to reduce costs and complications, appropriate clinical protocol of contrast media, more supervision on medical residents and contrast infusion pumps, as well as a periodic evaluation study are highly recommended.

Keywords: Contrast media, Irrational use, Visipaque, Cost, Drug utilization reviews

Introduction

About one-third of the annual hospital budget is spent on providing materials and supplies, including medicines (1). Therefore, irrational use of medicine is a major concern worldwide. Irrational drug use may also lead to increased costs in medical care, and side effects and patient mortality(2). Hence, in recent years, Drug Utilization Reviews (DUR) have become a potential tool to be used in the evaluation of health system. DUR are defined use of drugs in a society, with special reliance on the resulting medical, social and economic consequences (2).

Visipaque is an iso-osmolar contrast media with the chemical name of iodixanol, which is used for Percutaneous Coronary Intervention (PCI). Also, visipaque has approved indication for angiocardiography (left ventriculography and selective coronary arteriography), cerebral arteriography, peripheral arteriography, visceral arteriography. Dose is individualized based on injection site and study type, but maximum recommended total dose of iodine is not more than 80 grams (250 mL for visipaque 320 mg/ml). Dose adjustment in renal impairment is not necessary. In general, it is desirable to limit the contrast media to less than 30 mL for a diagnostic procedure and less than 100 mL for an interventional procedure (3-5). The most important side effect of contrast media is acute kidney injury which might be due to an increased volume of contrast media during the procedure. It is associated with prolonged

hospital stay, increased costs, and both short- and long-term mortality(6). Therefore, irrational use of this drug can affect the direct and indirect costs of the hospital. The cost of visipaque injectable solution (320 mg/ml) is around $15 for a supply of 50 milliliters in Iran. Based on the ABC-VED (always, better, control - vital, essential and desirable) matrix analysis(7), visipaque® was categorized in category (AV) in our hospital.

This study aimed to analyze and evaluate the rational use of contrast media in patients undergoing PCI in a teaching heart hospital, to provide an overview of the volume of contrast media in each patient, and finally estimate the amount of contrast media based on the standard limits. Also as part of DUR study, we evaluated patients' safety profile and monitoring pattern.

Materials and Methods

This retrospective observational study was conducted by reviewing medical records and Hospital Information System (HIS) of 100 admitted patients aged 18 to 80 years old undergoing elective PCI who received visipaque® (320 mg/ml, 50 mL) during February 2016 to January 2017 in angiography wards of Fatemah Zahra Teaching Heart Hospital, Sari, Iran. We also excluded patients who died during PCI or patients undergoing hemodialysis. It was approved by the Ethics Committee of Mazandaran University of Medical Sciences (IR.mazums.rec.1395.2564).

Demographic data (age, gender, weight, cause of admission), contrast media information (type, volume, and dose), indication of PCI, Serum Creatinine (SCr), and length of stay in hospital were collected and recorded. Then, we calculated the Maximum Contrast Dose (MCD) for each patient by using the formula proposed by Cigarroa and colleagues (8): MCD (mL) :(5 × body weight [kg]) divided by SCr (mg/dl) (8).

We determined the contrast ratio by divided the administered amount of contrast media by the MCD. Therefore the patients were split into two categories of contrast ratio ≥ 1 and contrast ratio < 1. The risk of contrast-induced nephropathy was evaluated across use of a Volume (V) of Contrast to Creatinine Clearance (CrCl) (V/CrCl) ratio and Mehran risk score(9, 10). A risk score for the prediction of Contrast Induced Nephropathy (CIN) after PCI was reported by Mehran et al, that risk score includes hypotension (5 points, if systolic blood pressure <80 mmHg for at least 1 h requiring inotropic support), use of intra-aortic balloon pump (5 points), congestive heart failure 5 points, if class III/IV by New York Heart Association classification or history of pulmonary edema), age (4 points, if >75 years), anemia (3 points, if hematocrit <39% for men and <36% for women), diabetes mellitus (3 points), contrast media volume 1 point per 100 mL), and estimated glomerular filtration rate GFR; GFR in ml/min per 1.73 m2; 2 points, if GFR 60 to 40 points, 4 points if GFR 40 to 20; 6 points, if GFR <20 ml/min). A risk score of <6, 6 to 10, 11 to 6, and >16 indicates a risk for CIN of 7.5%, 14%, 26%, and 57%, respectively. We estimated creatinine clearance by applying the Cockcroft–Gault formula to the SCr concentration (11). To evaluate the proper dosage of the visipaque in each indication, we use different references and finally double-checked with our expert panel team (Table 1).

Data Analysis: Data were gathered and analyzed using the statistical software SPSS V. 19. The qualitative variables were recorded using frequency and percentage and the quantitative ones were recorded using mean and standard deviation. Besides, the correlation between the quantitative variables was evaluated through the spearman test. The Chi-square test and Fisher's exact test were also used to compare the two qualitative variables. $P<0.05$ was considered as a significance difference.

Table 1. Iodixanol dosage in different references

www.drugs.com	Right Coronary Artery 3 to 8 mL (320 mgI/ml) Left Coronary Artery 3 to 10 mL (320 mgI/ml) Left Ventricle 20 to 45 mL (320 mgI/ml) Max Total Dose: Usually not to exceed 200 mL
www.uptodate.com	Angiocardiography (left ventriculography and selective coronary arteriography), cerebral arteriography, peripheral arteriography, visceral arteriography: Intra-arterial: Iodixanol 320 mg iodine/mL: Dose individualized based on injection site and study type; refer to product labeling. Maximum recommended total dose of iodine: 80 g
https://reference.medscape.com	Intra-arterial administration (arteriography) • Carotid arteries: 10-14 mL • Verterbral arteries: 10-12 mL • Right coronary artery: 3-8 mL • Left coronary artery: 3-10 mL • Left ventricle: 20-45 mL • Renal arteries: 8-18 mL • Aortography: 30-70 mL • Major aorta branch: 10-70 mL • Peripheral arteries: 15-30 mL • Aortofermoral runoffs: 20-90 mL

Results

Out of the100 patients included in this study, sixty-nine of them were male. The mean age of patients was 58.74 ± 10.79 years old (range 18–80 years). One patient died after the PCI in the hospital. The patients' basic demographic and clinical characteristics are shown in Table 2. The mean duration of hospitalization was 12 ± 9 days (range 2–22 days). The amount of contrast media administered ranged from 200 to 600 mL (Mean ± SD = 348 ± 80 mL). In 55% of the patients visipaque was administered more than 250 mL (80 gr). When we adjusted contrast volume for patient based on weight and SCr by Cigarroa and colleagues' formula, MCD was in excess in 57% of patients, and also ten (10%) patients received contrast volume 1.5 times higher than the MCD. Overall, for 100 patients, about six liters more of the contrast agent were used than standard values with a cost estimated around $2,000.

Table 2 shows baseline, clinical and procedural characteristics in two groups based on contrast ratio. Patients with a contrast ratio greater than 1 experienced more complications such as higher risk of CIN and longer hospitalization following PCI.

In 90% of hospitalized patients, Mehran risk score was lower than 11points, but it is notable that patients with higher Mehran risk-score at the baseline received a greater amount of contrast media (contrast ratio>1) Table 2. Baseline SCr was performed for all patients, the mean SCr concentrations and CrCl were 1.015 ± 0.22 mg/ml and 86.98±26.13 ml/min respectively. Only 25 patients were evaluated with SCr after PCI and in 11 (44%) of these patients SCr increased and 3 (12%) patients developed CI-AKI. The mean volume of visipaque used for this group of patients was 433.33 mL.

Table 2. Patient and procedure characteristics

Variable		**Contrast Ratio**		***P***
		<1	≥1	
N		43%	57%	
Sex	**Male**	32%	37%	
	Female	11%	20%	0.38
Year		57.95 ± 10.64	59.04 ± 11.41	0.63
Weight		77.60 ± 11.43	78.91 ± 13.08	0.61
Diagnose	**CAD**	32%	44%	
	MI	11%	13%	0.88
Smoking		10%	9%	0.51
Diabetes Mellitus		14%	24%	0.33
Hypertension		21%	25%	0.23
Potassium		4.40 ± 0.37	4.35 ± 0.42	0.44
Hemoglobin		12.38 ± 1.76	12.30 ± 1.62	0.79
Patient Mehran Risk Score		4.55 ± 2.35	6.24 ± 2.87	0.02*
GFR(Before PCI ml/min)		90.03 ± 22.49	84.56 ± 28.54	0.30
SCr before PCI mg/dl		0.97 ± 0.21	1.04 ± 0.23	0.12
CI-AKI		0	3	N/A
Maximum Contrast Dose (MCD)		278.65 ± 13.16	273.61 ± 21.48	0.15
Administered Amount of Contrast Media		283.72 ± 35.72	396.46 ± 69.34	<0.001
Hospital Stay		4.26 ± 2.52	5.82 ± 4.30	0.025*

CAD: Coronary Artery Disease; MI : Mycardial Infraction; GFR :Glomerular Filtration Rate; SCr: Serum Creatinine; PCI: Percutaneous Coronary Intervention; CI-AKI: Contrast-Induced Acute Kidney Injury; MCD: Maximum Contrast Dose
*P<0.05: significant difference

Discussion

To our knowledge, this study was the first investigation on the rational use of contrast agent with specific focus on calculating the extra volume of contrast media based on MCD and calculation of extra financial costs imposed on health systems.

Visipaque (iodixanol) is in a group of drugs called radiopaque (RAY dee oh payk) contrast agents. This medicine contains iodine, a substance that absorbs x-rays. Radiopaque contrast agents are used to allow blood vessels, organs, and other non-bony tissues to be seen more clearly on a CT scan or other radiologic (x-ray) examination. Visipaque is used to help diagnose certain disorders of the brain, blood vessels, heart, kidneys, and other internal organs. It is significantly more expensive than the previously available agents. Maximum recommended total dose of iodine is 80 gram. The cost of visipaque injectable solution (320 mg/ml) is around $15 for a supply of 50 mL in Iran.

In this study the mean volume used was 350 mL which is significantly higher than the maximum recommended dose of iodixanol (250 mL for visipaque 320 mg/ml). We found that in 57% patients, visipaque was administrated more than 250 mL (80 gr). Therefore, based on MCD for each patient, about 6000 mL of additional visipaque was used for the 100 patients. It can be said that close to an extra 60 mL (one vial of 50 mL) visipaque was used for each patient. The cost of this amount was 2000 dollars for 100 patients. It is important to know that more than 2000 PCI's are performed in this hospital annually.

Several studies have reported the prescription of more than the maximum standard volume of contrast media in PCI. In comparison with existing studies, in our research, the volume of contrast media was more than in the others. In Mehran et al study the mean volume of the contrast media used was 260.9 ± 122 mL for 5571patients undergoing the PCI (9). Vallero et al. reported average of 203 mL (mean) of contrast media for 100 patients undergoing angioplasty (12). In Al-Harthi et al study, Out of 144 patients who were enrolled 8 patients (5.6%) received a higher contrast media than the MCD (10). In A Mautone et al study, the results revealed that 20% of the patients received more contrast media than the MCD (13). And in Marenzi et al. study; approximately 23% of 561 patients had received more of this medicine than the MCD (14).

Renal failure is the most common complication following contrast media induced specially among patients undergoing PCI, since they are mostly of elderly age and because of their past medical history (diabetes, etc.) (15). There is an association between contrast volume and the presence of CIN in patients. In 1989, Cigarroa et al (8), described how adherence to a formula for contrast media could be used to significantly reduce the rates of CIN. The study showed that the incidence of CIN would be related to the dose of contrast agent and inversely proportional to SCr. Their formula [contrast media limit= 5 mL of contrast per kilogram body weight/SCr (mg/dL), maximum dose of 300 mL] was prospectively applied. Only 2% of those who remained under the limit developed CIN, while 21% of those exceeding the limit developed it.

Multiple studies have shown that an increased volume of contrast media is associated with the incidence of CIN (10, 16, 17). Mehran et al. presented a simple risk score for prediction of contrast-induced nephropathy after PCI (9). Mehran study revealed that each 100 mL of contrast media could be raised one point in the Mehran contrast nephropathy risk score. Rihal et al study also revealed that each 100 mL increase in the contrast volume was accompanied by a 12% rise in the risk of CIN (18).

In Freeman et al study it was found that increasing the amount of contrast media, higher than the MAD, could cause a six times more risk of CIN (19). In a study by Laskey et al, the Mean ± SD of contrast volume in developed AKI patients was 255 ± 124 mL, while those who did not develop AKI received 224 ± 112 mL (P=0.06)(20). In the present study, 55% and 35% of the patients had received contrast media more than 300 mL and 400 mL respectively that could be an important risk factor for CIN.

Since only 25 % of patients was evaluated SCr after the procedure, it is not possible to estimate the prevalence of CIN precisely. Out of 25 patients, the incidence of CIN was 12% (3 patients). The interesting point is all 3 patients were in the contrast ratio group higher than 1.

This finding may be due to the fact that our hospital is a teaching hospital. Another reason is the irrational use of iodixanol and not using infusion pumps for contrast media in our center.

Conclusion

Iodixanol protocol in our teaching hospital required modification. It is necessary to revise and implement standard guidelines to reduce inappropriate iodixanol use and costs.

This study was the first research on the rational use of contrast media and evaluation of the associated costs although we did not calculate the indirect costs of mortality and morbidity. Because of the high costs estimated for the illogical use of contrast media, further monitoring and training in this field can be helpful. Using an infusion pump device in order to prevent overconsumption and more supervision on medical residents during procedures is recommended.

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Authors' contributions

Marziye Jafari, Gohar Eslami, Babak Bagheri: study design and supervisors; Shirin Asghari Vaskasi: Thesis project and data gathering; Shafagh Eslami: data analysis and manuscript writhing.

Conflicts of interests

The authors declared no conflict of interest.

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