

Hemodynamic effects of contrast media and its adverse effects in Western Rajasthan: an observational study

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ABSTRACT

Background: This study was aimed to investigate the hemodynamic effects of CT scan contrast media on pulse rate and blood pressure as well as identify the possible adverse drug reactions occurring after administration of contrast media.

Methods: Information of patients such as age, sex, diagnosis, prescribed body part for CT scan, amount of contrast media and route of administration of contrast media were collected. Pulse and blood pressure were measured three times, before administration of iohexol or diatrizoate sodium; after 5 min and 1 hr administration of iohexol; after 1 hr and 2 hr starting of administration of diatrizoate sodium. ADR occurring after contrast media administration were observed.

Results: Before Iohexol administration, SBP was 126.85 ± 18.47 mmHg, which increased by 129.92 ± 20.51 and 128.24 ± 19.89 mmHg after 5 min. and 1 hr respectively after administration. Whereas before iohexol administration, DBP was 81.28 ± 11.5 mmHg, which was decreased by 80.58 ± 13.03 and 78.90 ± 13.15 mmHg after administration. The p-value for PR, pre-iohexol vs 1 hr post-iohexol was highly significant. Before Diatrizoate Sodium administration, SBP was 128.84 ± 17.64 mmHg, that was decreased with 126.23 ± 17.92 and 124.15 ± 17.04 mmHg after administration. On the other hand, DBP was 81 ± 11.99 mmHg which was decreased with 80.23 ± 11.07 and 79.84 ± 11.31 mmHg by Diatrizoate Sodium administration. P-value for SBP, DBP, and PR in various comparison of diatrizoate sodium administration was insignificant as well as total 18 ADRs were recorded post diatrizoate sodium and iohexol administration.

Conclusions: Present study result demonstrates PR was significantly increased by administration of iohexol but not that much due to Diatrizoate Sodium especially after the 1 hr of iohexol administration. Although DBP decreased by both drugs, on the other hand, SBP increased by iohexol and decreased by Diatrizoate Sodium administration which was clinically insignificant. Although headache and giddiness were most common ADRs by both drugs.

Keywords: Adverse drug reactions, CT scan, Diatrizoate sodium, Iohexol

INTRODUCTION

Many advanced diagnostic techniques are used prior to the 90s, such as radiographic imaging intravascular iodinated contrast agents as the mainstay. In the subsequent years, a marked decrease of abdominal and cardiac contrast procedures is noticed in many referral institutions due to the advent of diagnostic ultrasound. Since the start of the twenty-first century, the use of computed tomography

(CT) and magnetic resonance imaging (MRI) have increased. The increased accessibility, enhanced applications, and minimal invasiveness of these techniques have made them currently a popular diagnostic modality in medical science. Intravascular and extra-vascular contrast medium are used in many of CT scan studies. Over the last few years, particularly with the advent of helical multislice CT machines, there has been a marked increase in diagnostic use of Computed tomography angiography

(CTA), the study of vascular structures by utilizing contrast agents during the CT examination and multi-phase angiography to investigate arterial and venous phases, as well as organ perfusion. There has been a dramatic increase in the use of intravascular and extravascular iodinated contrast agents again, because of the increased research and knowledge about the diagnostic advantages of these techniques.¹⁻³ Further, their potential side effects must be kept in mind in routine clinical practice.

There are different types of iodinated contrast agents used in diagnostic imaging, based on their physical and chemical properties. All the first generation agents belong to high-osmolar ionic monomers. There is an increased rate of adverse reactions due to the high osmolality of these agents, so the safer second and third generation agents have replaced them.⁴ The low osmolar, non-ionic monomer second generation iodinated compounds (iopamidol and iohexol) with improved vascular tolerability and fewer side effects are most commonly used. The iodine content of a contrast medium is directly related to its radio-opacity, therefore the successive generations of contrast media have been developed with a goal to maximize the iodine content but minimize the osmolality of the resulting solution. The safest contrast agents reported till date are the third generation iodinated contrast media (Iodixanol and iotrolan) which are iso-osmolar, non-ionic dimers. However, they have limited use in human patients at risk of contrast-induced nephrotoxicity (CIN) and in particular those patients with severe renal insufficiency because of their high costs.⁵⁻⁷ Though some other reports have contrast findings and they show no difference between second and third generation contrast agents to induce CIN.⁸

There has been an extensive reporting and investigation of adverse reactions due to iodinated intravenous contrast media.^{4,8-11} The physical and chemical properties can be attributed to their side effects. Side effects can be divided into non-anaphylactoid, anaphylactoid and delayed. Pulmonary edema, cardiac arrhythmias, nausea, seizures, and renal failure are the non-anaphylactoid reactions while Urticaria, laryngeal edema and bronchospasm the anaphylactoid reactions. This is not stimulated by an immunoglobulin E-mediated response and so is not true anaphylaxis and it may also occur during the first exposure to the agent. Although, the treatment is the same as for an anaphylactic reaction. The above reactions appear within 1-3 minutes whereas delayed reactions may occur up to 6 hours after exposure which include fever, pruritis, arthralgia, headache, nausea, and vomiting.⁴

Contrast materials, also called contrast agents or contrast media, are used to improve pictures of the inside of the body produced by x-rays, computed tomography (CT), magnetic resonance (MR) imaging, and ultrasound. Moreover, the radiologist can also distinguish between normal conditions and abnormal conditions using contrast materials. Contrast materials temporarily change the way

of x-rays or other imaging tools interact with the body and do not discolor internal organs permanently. When introduced into the body prior to an imaging exam, contrast materials make certain structures or tissues in the body appear different on the images than they would if no contrast material had been administered.¹² Contrast materials help distinguish or “contrast” selected areas of the body from surrounding tissue. By improving the visibility of specific organs, blood vessels or tissues, contrast materials helping in diagnosis. Route of administration of Contrast materials is oral, rectal or systemic by injecting into a blood vessel (vein or artery) or intrathecaly.¹³

Most iodinated contrast media are administered via vascular, whereas, several of these agents are administered via nonvascular routes during such procedures as gastrointestinal imaging, cystography, sialography, cystography, and hysterosalpingography.¹⁴ The non-ionic iodinated contrast media is increasing rapidly in the population, although the safety profiles of this contrast media have been recognized as the most important issue. Many studies have been performed to investigate the safety profiles of ionic and non-ionic iodinated contrast media.²⁻⁴ However, only very few studies of Indian patients have been performed, in which sample sizes are generally small that could not fully reflect the incidence and pattern of adverse drug reactions (ADRs) induced by contrast media in Indian patients.¹⁵

In this study, authors demonstrate the hemodynamic effects and adverse effects of contrast media in respect to blood pressure and pulse rate.

METHODS

Study design

This was an observational, noninterventive, and prospective study conducted with the Association with the Department of Pharmacology and Department of Radiology, Dr. S. N. Medical College, Jodhpur. In this study, we used the contrast media iohexol and diatrizoate sodium. This was a single-centric study conducted at Mahatma Gandhi Hospital Jodhpur, a tertiary care center in western Rajasthan. Contrast media preparation and administration were performed, heart rate and blood pressure monitored.

Study patients

A total of 75 patients aged between 18 years to 75 years were studied, those referred for contrast CT scan of the various regions (thorax, abdomen, head and CT angiography). Out of 75 patients, 45 were male and remaining 30 were female participants. All 75 participants received iohexol intravenously as a contrast media and out of 75, 26 participants also received oral contrast media (diatrizoate sodium) that was given 2 hours before the iohexol media.

Participants Age between 18 to 75 years were included in the study, in that pregnant females and bedridden patients were excluded in this study. Written consent was taken from all participants. After taking informed consent, participants were included in the study.

Contrast material administration protocol

We selected participants in whom iohexol was used as an intravenous contrast media and diatrizoate sodium as an oral contrast media. Contrast media were warmed at 37°C temperature before the administration. 80 mL iohexol were administered intravenously with 4 mL/sec (35 ml) Via 18- to the 20-gauge intravenous catheter. On the other hand, 60 ml diatrizoate sodium were mixed in 2 liters of water for preparation of oral contrast media and allow the participants to drink within 2 hr,

Observation and monitoring

Participants were divided into group A and group B on the basis of participant administrated with iohexol (IV) or both iohexol (IV) and diatrizoate sodium (orally) respectively. Observations and monitoring were based on the basis of these groups. In group A, blood pressure and pulse rate monitored within 5 minutes before the iohexol administration, after 5 minutes and 1 hr of iohexol

administration. In group B blood pressure and pulse rate were monitored, before the start of contrast media, 1 and 2 hr after started of oral contrast media administration then CT scan performed and again BP and pulse rate monitored after 5 min and 1 hr of Iohexol administration. Adverse drug reaction was monitored during this period and necessary clinical action was done if any reaction was observed.

RESULTS

Effect of iohexol on blood pressure and pulse rate

Before administering of iohexol IV, authors observed systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate (PR) were 126.85±18.47 mm Hg, 81.28±11.50 mm Hg, and 86.12 ±17.12/min respectively (Table 1). After administration of iohexol IV within 5 min, SBP and PR was increased which were 129.92±20.51 mm Hg and 89.94±15.28/min. This increased in SBP and PR were also observed after 1 hr showed in Table 1. Whereas DBP was decreased (80.58±13.03 mm Hg) after the 5min and decreased in DBP also observe after 1hr of administration, shown in Table 1. The observation of pulse rate was highly significant in respect to SBP and DBP after the 1hr of iohexol administration which was not observed in previous studies (Table 1).

Table 1: Effect of iohexol on blood pressure and pulse rate.

Parameters	Before (Mean±SD)	After 5min (Mean±SD)	After 1hr (Mean±SD)	P value		
				Before vs After 5 min	After 5min. vs After 1 hr	Before vs After 1 hr
SBP (mmHg)	126.85±18.47	129.92±20.51	128.24±19.89	0.337	0.610	0.658
DBP (mmHg)	81.28±11.50	80.58±13.03	78.90±13.15	0.730	0.433	0.241
PR Rate/minute	86.12±17.12	89.94±15.28	92.36±16.02	0.150	0.346	0.026*

* represent significant P value.

Table 2: Effect of Diatrizoate Sodium on blood pressure and pulse rate.

Parameters	Before (Mean±SD)	After 1hr (Mean±SD)	After 2hrs (Mean±SD)	P value		
				Before vs After 1 hr	Before vs After 2 hrs	After 1hr vs 2 hrs
SBP (mmHg)	128.84±17.64	126.23±17.92	124.15±17.04	0.938	0.726	0.670
DBP (mmHg)	81±11.99	80.23±11.07	79.84±11.31	0.811	0.722	0.901
Pulse Rate/ minute	83.34±13.78	85.38±14.47	85.11±14.36	0.605	0.652	0.946

Effects of diatrizoate sodium on blood pressure and pulse rate

Before administering of Diatrizoate Sodium (orally), authors observed SBP, DBP, and PR which were 128.84±17.64 mm Hg, 81±11.99 mm Hg, and 83.34±13.78/min respectively (Table 2). After administration of diatrizoate sodium, SBP and DBP were

decreased within 1 hr, which were 126.23±17.92 mm Hg and 80.23±11.07 mm Hg respectively, showed in Table 2. This decreased in SBP and DBP were nearly constant in following 2 hr after administration. On the other hand, PR was increased with 85.34±14.47/min and nearly constant in following 2 hr after the administration, showed in Table 2.

Adverse drug reaction

A total of 18 (24%) participants with ADRs were recorded out of 75 participants, among them, 9 (18%) and 5 (19.23%) were after administration of IV iohexol and diatrizoate sodium orally respectively, showed in Table 3. 4 (15.38%) ADRs were found after combined use of IV iohexol and diatrizoate sodium (orally).

Another side if we calculate it differently than 13 (17.33%) participants get ADRs out of 75 with iohexol administration and 9 (34.61%) out of 26 participants got the ADRs. So, the incidence of ADRs due to IV iohexol (17.33%) administration was less comparatively oral diatrizoate sodium (34.61%) administration (Table 3).

Table 3: Adverse drug reaction.

Type of contrast media	Total	ADR
IV (iohexol)	49 (65.33%)	9 (18.37%)
Oral (diatrizoate sodium) (before IV)	26 (34.67%)	5 (19.23%)
IV+ oral	26 (34.67%)	4 (15.38%)
Total	75	18 (24%)

Type of adverse drug reaction

Total 28 ADRs were found in 75 participants. These were headache (n=11), giddiness (n=8), vomiting (n=2), abdominal pain (n=2), flushing of skin (n=2), diarrhea (n=2), syncope (n=1). Headache (39.29%) was most common ADR. So, in this view headache and giddiness were most common ADRs (Table 4).

Table 4: Types of adverse drug reaction.

Type of ADR	Total	Percentage (%)
Headache	11	39.29
Giddiness	8	28.57
Vomiting	2	7.14
Abdomen pain	2	7.14
Syncope	1	3.57
Flushing of skin	2	7.14
Diarrhea	2	7.14
Total	28	100

Type of adverse drug reaction by using different contrast media

Total 28 ADRs were found in 75 participants. Among them, 14 ADRs occur after administration of Diatrizoate Sodium (orally). Out of these headache (n=2), giddiness (n=6), vomiting (n=2), abdominal pain (n=2) and diarrhea (n=2), showed in Table 5. Giddiness was most common ADR caused by Diatrizoate Sodium (23%). 14 ADRs occur after administration of iohexol (IV) out of this headache (n=9), giddiness (n=2), flushing of skin (n=2) and syncope (n=1). So, in the above view headache (12%) was most common ADRs which occurred after administration of IV

iohexol while giddiness (23.08%) was most common ADRs due to diatrizoate sodium (orally) (Table 5).

Table 5: Adverse drug reaction by using different contrast media.

Type of ADR	ORAL (diatrizoate sodium)	IV (iohexol)
Headache	2 (7.69%)	9 (12%)
Giddiness	6 (23.08%)	2 (2.67%)
Vomiting	2 (7.69%)	0
Abdomen pain	2 (7.69%)	0
Syncope	0	1 (1.335%)
Diarrhea	2 (7.69%)	0
Flushing of skin	0	2 (2.67%)
Total	14 (53.85%)	14 (18.67%)

DISCUSSION

The aim of the study was to evaluate the hemodynamic effects of CT scan contrast media on pulse rate and blood pressure as well as identify the possible adverse drug reactions occurring after administration of contrast media in patients visiting Radiology Department for contrast CT scan for that we observed 75 patients.

In present study post-diatrizoate sodium administration, SBP and DBP were decreased which was clinically insignificant, on the other hand, PR was increased after diatrizoate sodium administration, but it was clinically insignificant. While Hirschfeld et al, reported in left ventriculography, diatrizoate caused a significant increase in left ventricular end diastolic pressure, cardiac output, and corrected QT interval while causing a greater decrease in arterial pressure comparing to ioversol or iopamidol, following left coronary arteriography, diatrizoate caused a significant decrease in heart rate.¹⁶

Present study revealed the post iohexol administration SBP was increased but DBP was decreased, although this was clinically insignificant. While Ning et al, show that ferumoxylol is effective as an MR contrast agent and there are small but clinically insignificant fall in SBP and DBP post-contrast injection.¹⁷ Hayashi et al, found Intravenous Gadoxetate disodium (a weight-based dose) does not cause any changes in SpO₂ and heart rate.¹⁸

Present study showed, that pulse rate increase after 1hr of post iohexol administration was highly significant but increase in PR after 5 min of iohexol administration was insignificant. Which is not according to James et al, study, in that study they demonstrated that there were no clinically significant changes in heart rate, new rhythms or cardiac waveform morphology or AV conduction, either by IV or non-cardiac intraarterial injection of iosimenol. There are no such significant differences recorded between groups receiving iodixanol and those receiving Iosimenol.¹⁹

Present study shows that incidence of ADRs due to IV iohexol was 17.33% and diatrizoate sodium was 34.61% which was quite high. A mild headache and giddiness were most common ADRs due to iohexol and diatrizoate sodium administration, among this mild headache (12%) were most common ADRs which occurred due to IV Iohexol while giddiness (23.08%) was most common ADRs due to diatrizoate sodium (orally). Which was not according to Subathra et al, they demonstrated in their study, most common adverse reactions to contrast are nausea, vomiting, and rashes. Most of the reactions occur immediately after administration of contrast and mostly are mild to moderate in nature.²⁰ While Egbert et al, found in their study that delayed adverse reactions to contrast media are not rare but often not recognized as being linked with to contrast administration and maybe occasionally falsely attributed to other drugs. These side effects are sometimes problematic because the patient is usually without medical supervision.²¹

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