Adverse Reactions from Contrast Media in Patients Undergone Computed Tomography at the Department of Radiology, Srinagarind Hospital

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Abstract—Background: The incidence of adverse reactions to iodinated contrast media has risen. The dearth of reports on reactions to the administration of iso- and low-osmolar contrast media should be addressed. We, therefore, studied the profile of adverse reactions to iodinated contrast media at Srinagarind Hospital. Method: Between March and July, 2015, 1,101 patients from the Department of Radiology were observed and interviewed for the occurrence of adverse reactions. The patients were classified per Naranjo’s algorithm and through use of an adverse reactions questionnaire. Results: A total of 105 cases (9.5%) reported adverse reactions (57% male; 43% female); among whom 2% were iso-osmolar vs. 98% low-osmolar. Diagnoses included hepatoma and cholangiocarcinoma (24.8%), colorectal cancer (9.5%), breast cancer (5.7%), cervical cancer (3.8%), lung cancer (2.9%), bone cancer (1.9%), and others (51.5%). Underlying diseases included hypertension and diabetes mellitus type 2. Mild, moderate, and severe adverse reactions accounted for 92, 5 and 3%, respectively. The respective groups of escalating symptoms included (a) mild urticaria, itching, rash, nausea, vomiting, dizziness, and headache; (b) moderate hypertension, hypotension, dyspnea, tachycardia and bronchospasm; and (c) severe laryngeal edema, profound hypotension, and convulsions. All reactions could be anticipated per Naranjo’s algorithm. Conclusion: Mild to moderate adverse reactions to low-osmolar contrast media were most common and these occurred immediately after administration. For patient safety and better outcomes, improving the identification of patients likely to have an adverse reaction is essential.

Keywords—Adverse reactions, contrast media, computed tomography, iodinated contrast agents.

I. INTRODUCTION

The number of people receiving services at Srinagarind Hospital has increased annually, so that by 2013 it served 850,000 patients: a rise of 45,000 from the previous year [1]. Consequently, the hospital has had to improve its preparedness for the large number of incoming patients.

Currently, radiologic diagnosis with modalities (contrast media) plays a major role in modern medicine. Computed tomography (CT Scan) employs multiple X-ray slices, that pass through the body in various planes, creating 3D, cross-sectional, computer-generated images of the desired organ that can be viewed from various angles on screen. These images are used for assessing anatomy, detecting abnormalities, and diagnosing disease (including congenital disorders) and determining the status of infectious disorders, vascular tumors, and accidents. In conjunction with injection modalities (using iodine compounds), CT is invaluable for: (a) Detecting tumors in various organs; (b) determining tumor spread to lymph nodes; (c) assessing retention of blood in the brain, abdomen, and pelvis; (d) detecting coronary artery aneurysms and embolisms; and, (e) assessing bone disorders including, arthritis or fractures. Owing to these multiple uses and evident benefits, the respective number of patients receiving CT Scan in 1998 and 1999 was 6,645 and 7,680, which rose to 9,953 in 2012 [1].

Modalities using iodine (i.e., iodinated contrast media) help to visualize kidneys, blood vessels, gall bladder, bile ducts, urinary tract, and lymph nodes, but careful consideration must be given to the dosages given as the contrast media are delivered directly into the body (i.e., orally, rectally, intravenously, or through a colostrum line), and there can be adverse reactions.

Idiosyncratic or general- reactions occur within 20 minutes after injection [2] (i.e., anaphylactic shock). An immunoglobulin E (IgE adverse reaction has non-specific symptoms but these directly affect organs (including heart rate and low blood pressure). Since modalities can exacerbate the severity of disease, people with medical conditions (i.e., cardiac arrhythmias and ischemic) are at risk. The deterioration of the kidney due to the adverse non-specific effects from contrast modalities (i.e., contrast induced nephropathy, CIN) can be categorized into 3 levels (mild, moderate, and serious). Mild symptoms include rash, allergic reactions, distributed generally, and followed by itching, nausea, vomiting, sweating, coughing and dizziness. Moderate symptoms include rash all over the body, facial swelling, bronchoconstriction, tachycardia, palpitations, wheezing, abdominal pain, abdominal cramp requiring diagnosis and immediate treatment. Serious symptoms include severe cardiac arrhythmias, low blood pressure, bronchospasm, severe throat swelling, pneumonia, seizures, coma and possibly death. This category could also have non-idiosyncratic reactions and organ-specific types of adverse reactions caused by a direct effect on cell structure. All patients should be closely monitored.
One of the mechanisms of actions from contrast media may affect the results of enzymes which stimulate the complementary system while other causes have different potential from mild to life-threatening that affect organs (i.e., bradycardia, hypotension). Vasovagal reactions induce the parasympathetic system and may be associated with symptoms of the autonomic nervous system including nausea, vomiting, diarrhea, sweating, confusion, a reduction in the rate of discharge from the sino-atrial node and atrial-ventricular node making the heart beat slower. The peripheral expansion causes low blood pressure, cardiovascular reactions, including severe hypotension and bradycardia. These symptoms are caused by compounds that act on the heart and blood vessels caused by anaphylactoid reaction from iodinated contrast media.

Accidental extravasation or contrast extravasation is caused by contrast media injection leakage from the vessel puncture site or leaks into the tissue around vein. Contrast extravasation is a well-recognized complication; the respective reported frequencies where power injectors were used in three large CT series was 0.25% (56/22,254), 0.7% (475/69,657), and 0.9% (48/5,106) [3]-[5].

In the current study, reactions were not regarded adverse reactions from contrast extravasation as they occurred after administration of the contrast media. Nueaithong reviewed 2,176 patients injected with contrast media for the diagnosis of special urology and found 9.3 percent of the patients had adverse reactions: 8.9% mild, 0.4% moderate, and no severe adverse reactions [6]. In another study by a Japanese committee on the safety of contrast media, of 337,647 adverse reactions [6]. In another study by a Japanese committee on the safety of contrast media, of 337,647 adverse reactions: 8.9% mild, 0.4% moderate, and no severe reactions to the administration of iso- and low-osmolar contrast media [7]. Few studies provide frequencies where power injectors were used in three large CT series was 0.25% (56/22,254), 0.7% (475/69,657), and 0.9% (48/5,106) [3]-[5].

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A total of 1,101 patients were included in the study: 623 (57%) males and 478 (43%) females. Adverse reactions were reported by 105 cases (9.5%). The mean age ± SD of all patients was 55.5±15.8 vs. 54.7±11.6 for those who developed adverse reactions. Most of those having an adverse reaction from contrast media were between 51 and 60 years of age (33.34%). The other respective age ranges (and proportion suffering adverse reactions) were 61-70 (26.7%), 41-50 (21%), 31-40 (9.5%), 20-30 (4.8%), and 70 and over (4.8%). The medical histories indicated the rank of medications being taken was: Anti-diabetic medications, anti-hypertensives, cardiovascular medications, anti-hyper/hypothyroid medications, anti-epileptics, and anti-virals. The rank of diagnosed diseases included: Hepatoma and cholangiocarcinoma, abdominal and stomach cancer, lung cancer, colorectal cancer, cervical cancer, breast cancer, brain cancer, kidney cancer, gallbladder cancer, cardiovascular disease, bone cancer, and others. The rank of diseases associated with an adverse reaction included: Hepatoma and
cholangiocarcinoma (24.8%), colorectal cancer (9.5%), breast cancer (5.7%), cervical cancer (3.8%), lung cancer (2.9%), bone cancer (1.9%), and others (51.5%). There was no significant difference in the occurrence/non-occurrence of adverse reactions to iodinated contrast media due to sex, mean age, or medical history (Table I).

Among the 1,101 cases who received contrast media, 105 had adverse reactions. Among those who with an adverse reaction from contrast media for diagnosis, 2% were iso-osmolar and 98% low-osmolar. In the current study, the respective rank of those having majority who had an adverse reaction from iodinated contrast media using low-osmolarity for diagnosis were iopromide (31%), iohexol (26%), iopamidol (21%), iobitridol (20%), and iso-osmolarity as ioxidanol (2%), (Table II).

105 of 1,101 patient’s reactions were classified using Naranjo’s algorithm for an adverse reaction with contrast media; then, they were assessed per their symptoms using specific questionnaire administered by a pharmacist. Their symptoms were assessed; all reactions were deemed to be probable. The respective incidence of mild, moderate and severe adverse reactions accounted was 92, 5, and 3%. The most common adverse reaction after iodinated contrast media administration was immediate; occurring within an hour (both mild and severe). Incidences of delayed adverse reactions (occurring hours to weeks after the administration of ionated contrast media) are classified in (Table III). These reactions are usually self-limiting and cutaneous though they can be classified as moderate adverse reactions.

The respective groups of escalating symptoms included: mild—urticaria, itching, rash, nausea, vomiting, dizziness, and headache; moderate—hypertension, hypotension, dyspnea, tachycardia and bronchospasm; and, severe—laryngeal edema, profound hypotension, and convulsions (Table IV). The most common adverse reactions included: cutaneous urticaria, itching, and immediate MP rash. A few cases had nausea/vomiting, dizziness, and headache. Among the severe reactions, symptoms included laryngeal edema, profound hypotension, and convulsions, but the incidence was low compared to mild adverse reactions.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Symptoms*</th>
<th>Amount</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Urticaria</td>
<td>82</td>
<td>78.1</td>
</tr>
<tr>
<td></td>
<td>Itching</td>
<td>19</td>
<td>18.1</td>
</tr>
<tr>
<td></td>
<td>MP rash</td>
<td>18</td>
<td>17.14</td>
</tr>
<tr>
<td></td>
<td>Nausea / Vomiting</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>Hypertension</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
<td>1</td>
<td>≤1.0</td>
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<tr>
<td></td>
<td>Dyspnea</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td></td>
<td>Tachycardia</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td></td>
<td>Bronchospasm</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td>Severe</td>
<td>Laryngeal edema</td>
<td>2</td>
<td>1.9</td>
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<tr>
<td></td>
<td>Profound hypotension</td>
<td>1</td>
<td>≤1.0</td>
</tr>
<tr>
<td></td>
<td>Convulsions</td>
<td>2</td>
<td>1.9</td>
</tr>
</tbody>
</table>

* Patient could have more than one symptom

IV. DISCUSSION

The present study comprised out-patients from the Radiology Department of Srinagarind Hospital. We focused on patients who developed an adverse reaction due to administration of non-iodinated contrast media. All other reports of adverse reactions from contrast media were due to non-iodinated contrast media over against the 9.5% in our study. Several studies reported the prevalence of adverse reactions from both iodinated and non-iodinated contrast media [8]-[12]. Reports on the characteristics of patients after contrast media administration with an adverse event indicate no significant difference among adverse reactions vis-à-vis particularly sex and age. In an Indian study, neither sex nor age yielded any significant association with development of adverse reactions [10].

In the current study, adverse reactions were classified into 3 types (i.e., mild, moderate, and serious). The most common adverse reactions were mild (i.e., urticaria, itching, MP rash, nausea, vomiting, dizziness, and headache) and these developed within 30 minutes of administration; these were also classified as immediate. Some studies of low osmolarity contrast media [6]-[11] found that less than 3% of patients had reactions which were immediate.

The reported reactions include mild reactions such as urticaria, itching, MP rash, and nausea. Moderate and severe reactions include bronchospasm, cardiac arrhythmia, and loss of consciousness. Mortality due to contrast media reactions is low or ≤1 one death per 100,000 patients [7], [13], [14]. Incidence of immediate reactions to nonionic contrast media ranged from mild (i.e., 3%) to severe (i.e., 0.01–0.04%) [12]. Non-ionic agents are associated with a decreased risk of adverse reactions [11]. The prevalence of adverse reaction with ionic contrast media was 12.7% compared to 3.13% when using non-ionic contrast media [2], [6], [12].
comparison, high-osmolality contrast media have 5-8 times the osmolality of plasma. At present, both low-osmolality and iso-osmolality are used in diagnosis increasingly. The incidences of mild and moderate contrast media reactions are higher for high osmolality contrast media (6-8%) than low osmolality contrast media 0.2% [14], [15]. Similarly, reactions are infrequent and range between 5% and 12% for high osmolality and low osmolality (1-3%) for contrast media [15], [16].

Although, our study used non-iodinated contrast media, the most common reactions were mild albeit immediate reactions are akin to hypersensitivity reactions; including both E and non-Ig E-mediated anaphylaxis, with activation of mast cells, coagulation, kinin and complementary mechanisms, (i.e. inhibition of enzymes, and platelet aggregation) [17]. As for severe adverse reactions, one case was given iopamidol and 2 cases were given iopromide. The symptoms included anaphylactic shock, severe hypotension, confusion, dyspnea, desaturation and generalized urticaria [17]-[19]. Finally, anti-histamines are initially used to manage common reactions from iodinated contrast media in mild reactions. Severe reactions [20], [21] are treated by guidelines and a hospital multidisciplinary team.

V. CONCLUSION

Mild to moderate adverse reactions to low-osmolarity contrast media were the most common and these occurred immediately after administration of the media. Improving the identification of patients likely to have an adverse reaction is critical to avoiding life-threatening outcomes.

REFERENCES