Immediate Adverse Reactions to Intravenous Iodinated Contrast Media inComputed Tomography

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This exploratory-descriptive, non-experimental quantitative research aimed to learn about immediate adverse reactions to intravenous iodinated contrast media in hospitalized patients submitted to computed tomography at a teaching hospital in the South of Brazil. During the study period, all adverse reactions showed mild intensity, at a frequency of 12.5% with ionic iodinated contrast media, and 1% with non-ionic contrast agent. The extravasation of contrast occurred in 2.2% of the injections in a peripheral vein without complications in any of the cases. The results are within the limits cited in international literature and suggest that tomography service professionals should know their own rates of adverse reactions to iodinated contrast agent, as well as the conditions in which they occur, in order to obtain evidence to evaluate the respective care delivery processes.

DESCRIPTORS: contrast media/adverse effects; extravasation of diagnostic and therapeutic materials/nursing; tomography spiral computed; drug monitoring

Reacciones Adversas Inmediatas Al Contraste Yodado Intravenoso En Tomografía Computarizada

Investigación cuantitativa del tipo exploratorio-descriptivo, de carácter no experimental. El objetivo consistía en conocer las reacciones adversas inmediatas al contraste yodado intravenoso en pacientes internados, sometidos a tomografía computarizada en un hospital escuela del sur de Brasil. Durante el período del estudio, todas las reacciones adversas tuvieron intensidad leve y una frecuencia del 12,5% con la utilización del contraste yodado iónico, y 1% con contraste no iónico. La extravasación del contraste ocurrió en un 2,2% de las inyecciones en vena periférica, no ocasionando complicaciones en ninguno de los casos. Los índices evidenciados en el presente estudio se mantuvieron dentro de los límites que constan en la revisión de literatura y, entre las recomendaciones, se sugiere que los servicios de tomografía conozcan los propios índices de reacciones adversas al contraste yodado y las condiciones en que ocurren, con la finalidad de obtener evidencias para evaluación de los respectivos procesos asistenciales.

DESCRIPTORES: medios de contraste/efectos adversos; extravasación de materiales terapéuticos y diagnósticos/enfermería; tomografía computarizada espíral; monitoreo de drogas

Reações Adversas Imediatas ao Contraste Iodado Intravenoso Em Tomografia Computadorizada

Pesquisa quantitativa, exploratória-descritiva, de caráter não experimental, com o objetivo de conhecer as reações adversas inmediatas ao contraste iodado intravenoso em pacientes hospitalizados, submetidos a tomografia computadorizada num hospital-escola no Sul do Brasil. Durante o período de estudo, todas as reações adversas manifestaram-se na intensidade leve, com frequência de 12,5% com o uso de contraste iodado iônico e 1% com contraste não iônico. Extravasamento do meio radiopaco ocorreu em 2,2% das injeções em veia periférica, não havendo complicações em nenhum dos casos. Os resultados encontram-se dentro dos limites citados na literatura internacional e sugere-se que os serviços de tomografia conheçam as próprias taxas de reações adversas ao contraste iodado e as condições em que elas ocorrem, a fim de obter evidências para a avaliação dos respectivos processos assistenciais.

DESCRITORES: meios de contraste/efeitos adversos; extravasamento de materiais terapêuticos e diagnósticos; enfermagem; tomografia computadorizada espíral; monitoramento de medicamentos
INTRODUCTION

Adverse reactions to iodinated contrast medium happen relatively frequently in daily work at imaging units, and their occurrence can range from light forms to life-threatening events. International studies indicate that these events occur in between 0.2 and 12.7% of contrast injections, depending on the type and characteristics of the radiopaque substance that is used\(^1\text{-}^2\). However, there are no national publications about the frequency of these reactions in Brazilian radiology services. Thus, this research aimed to find out about immediate adverse reactions presented by hospitalized patients submitted to computed tomography (CT) with intravenous iodinated contrast, at a teaching hospital in the South of Brazil. A further goal was to identify the frequency of these events and establish a parallel with results from international references. This knowledge can support care and management decisions, contributing to more qualified and specialized care delivery to clients submitted to tomographies.

LITERATURE REVIEW

Iodinated contrast is a radiopaque substance used in radiology exams like computed tomography, which is widely used for diagnostic purposes. Although it improves the visualization of anatomic structures during the exam, this substance can provoke unwanted adverse effects, mainly due to the contrast’s high osmolality in relation to blood\(^3\). Ionic iodinated contrast is dissociated in ions when solved and its osmolality is higher than that of so-called non-ionic compounds, which do not dissociate into electrically-loaded particles. Therefore, the non-ionic medium is safer and has a better tolerability, but its high cost impedes its indiscriminate use\(^4\text{-}^5\).

Adverse reactions (AR) or unwanted effects resulting from iodinated contrast administration are generally classified, in terms of etiology, in anaphylactoid and chemotoxic reactions. Anaphylactoid or idiosyncratic reactions do not depend on the administered contrast dose and are similar to allergic reactions, taking the form of urticaria, nasal cold, hypotension accompanied by tachycardia, bronchial spasm and laryngeal edema, as well as more intense manifestations like shock and severe respiratory failure. Chemotoxic or non-idiosyncratic reactions are dose-dependent and related to the contrast’s physical-chemical characteristics, such as osmolality and ionicity. Their signs and symptoms can include feelings of heat, nausea and vomiting, heart arrhythmia, hypertension, renal failure and convulsions, among others\(^4\). As to severity level, reactions are classified as light, when they pass spontaneously and no therapy is needed; moderate, when the reaction recedes through medication intervention, without needing hospitalization; and severe, when life-support measures and hospitalization are required\(^2\text{-}^4\). Adverse reactions are called acute when they occur within 30 minutes after contrast administration and late when they occur after 30 minutes and up to seven days later\(^5\). Risk factors associated with the occurrence of adverse reactions to iodinated contrast include previous history of adverse reactions to radiopaque medium, history of asthma or allergies, heart arrhythmias, ischemic heart disease, general weakness, impaired communication, anxiety, kidney failure, extreme age and concomitant use of some drugs, such as beta blockers, metformin and nephrotoxic agents\(^4\text{-}^6\). The frequency of adverse events associated with iodinated contrast ranges between 2.2 and 12.7% when ionic medium is used and between 0.2 and 3.1% when non-ionic contrast is used\(^1\text{-}^2\text{-}^7\).

Iodinated contrast extravasation is considered a local adverse effect of intravenous radiopaque substance administration. Most extravasations involve small volumes of less than 10 ml, evolving without complications; however, large volumes of 50 ml or more can damage neighboring tissues of the puncture site and, rarely, compartmental syndrome\(^6\). According to international literature\(^2\text{-}^8\text{-}^10\), the frequency of radiopaque medium extravasation varies between 0.3% and 3.6%. Some risk factors for the occurrence of contrast extravasation are fragility of the venous network, venipunctures with metallic needles in comparison with plastic catheters, previously catheterized veins, multiple puncture attempts, impaired communication, extreme age, earlier or current chemotherapy or radiotherapy treatment\(^6\text{-}^11\).

The nursing team active in computed tomography services plays an important role in the prevention, detection and treatment of adverse effects caused by iodinated contrast use. At the research hospital, nursing examines the presence of risk factors for the occurrence of these reactions, provides
for venous access and injects the contrast agent. Moreover, nursing professionals identify signs of systemic or local adverse reactions and implement the treatment needed for each case. Hence, the monitoring of adverse events deriving from tomographies is a tool to assess care delivery at this service and an important care quality indicator.

**METHOD**

A quantitative, exploratory-descriptive and prospective study was carried out at the Radiology Service of the Porto Alegre Hospital de Clínicas (HCPA). This general public hospital belongs to the hospital network of the Brazilian Health Ministry and is academically affiliated with Rio Grande do Sul Federal University (UFRGS). The HCPA has approximately 830 beds and, every month, the Tomography Unit performs about 900 tomographic exams. This non-experimental research was favorably assessed by the Research Group and the Graduate Program at the institution through amendment 1 of Project GPPG 02-342. Data were collected through a registry framework, filled out manually by the nursing team during the service’s functioning hours (24/24), including all hospital patients who underwent contrasted CT between October 1st and December 10th 2004. After the exam, patients were assessed for the occurrence of immediate adverse reactions deriving from the use of intravenous iodinated contrast during the 30 minutes after the radiopaque medium was administered. At the end of the data collection period, a sample of 351 subjects was obtained, 161 of whom received ionic iodinated contrast (meglumine diatrizoate) and 190 received non-ionic iodinated contrast (ioversol). To study extravasation, only subjects who received the contract injection through peripheral venous access were included, totaling 317 patients.

Data were treated through descriptive and analytic statistics, using SPSS v. 12.0, EPI INFO v. 6 and PEPI v. 3. Chi-square and Fisher’s exact test were used to check for possible associations between variables, considering p<0.05 as significant, with a 95% confidence interval (CI).

Next, in the results section, findings related to extravasation of the radiopaque medium were described separately, as this is a local adverse effect for which different sample subject inclusion and exclusion criteria were adopted.

**IMMEDIATE ADVERSE REACTIONS**

In the group of 160 patients who received ionic iodinated contrast, we found 20 cases of immediate adverse reactions, corresponding to a frequency of 12.5% (CI95%:8.0%;18.3%). Eighty-five percent of reactions were anaphylactoid, mainly characterized by pruritic papules and, less frequently, by face hyperemia and sneezing. Chemotoxic reactions only took the form of vomiting. Among the 191 patients who received the non-ionic medium, only two cases presented an immediate adverse reactions, exclusively characterized by vomiting, corresponding to a reaction frequency of 1.0% (CI95%:0.2%;3.4%). This rate was significantly lower than when ionic contrast agent is used (p=0.000), supporting the assertion that the non-ionic medium, with lower osmolality, drastically reduces the risk of adverse reactions¹. Intensity of all events was light, with signs and symptoms receding spontaneously, and 54.6% of events started within the first ten minutes after contrast administration.

In Table 1, rates found in this study are compared with international references, showing no significant difference between these results and a Japanese research¹. That study included feeling hot as an adverse reaction, with a frequency of 2.29% for ionic medium and 0.92% for non-ionic medium, while that symptoms was not considered here. Other authors⁷ ignore not only feeling hot, but also the occurrence of vomiting. Therefore, when drawing a parallel with the results of that reference source, manifestations of vomiting were excluded. Result differences were significant for ionic iodinated contrast usage only; however, it should be highlighted that those researchers do not distinguish between light and moderate reactions, grouping them in one single category of adverse reactions. This means that, although this study found a higher rate of adverse events when ionic contrast was used, these events were less severe, as they only referred to light reactions.

Table 1 - Comparison between AR rates found in international publications and in this study

<table>
<thead>
<tr>
<th>Authors, year of publication</th>
<th>AR rate in the publication</th>
<th>AR rate in current study</th>
<th>Fisher's Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katayama, Yamaguchi, Koizuka, Takashima, Sasa, Matsuzawa, 1999*</td>
<td>ICM=12.66%</td>
<td>ICM=12.5%</td>
<td>p=0.961</td>
</tr>
<tr>
<td>Nonionic ICM=3.13%</td>
<td>Nonionic ICM=1.0%</td>
<td>p=0.098</td>
<td></td>
</tr>
<tr>
<td>Valls, Andia, Sánchez, 2003</td>
<td>ICM=2.2%</td>
<td>ICM=10.8%</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Moreno</td>
<td>MCI=3.0%</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>* ICM = Iodinated Contrast Medium</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
As to the contrast volume used for each exam, it was observed that the radiopaque substance dose, expressed in ml/kg, is not a determinant factor for the occurrence of adverse reactions in general, neither for ionic nor for non-ionic iodinated contrast.

Some studies\(^{[1-2,8]}\) have addressed the influence of the injection technique or contrast administration speed on the occurrence of adverse events, but these international research results are controversial. In this study, we found that automatic contrast injection significantly increased the occurrence of adverse reactions, but only in the ionic group: manual injection provoked AR in 3.6% of cases, while injections through an injection bomb resulted in 17.1% (\(p=0.013\)).

When considering the influence of some client-related variables, literature\(^{[1]}\) reports higher prevalence rates for all adverse reactions with both contrast types in the age range from 20 to 29 years, with a significant decrease in frequencies for each year added to the patient’s age. Hence, the younger the patient, the higher the probability of developing an immediate or late adverse reaction to iodinated contrast\(^{[12]}\). In fact, in this study, the frequency of reactions to the ionic medium decreased from the age of 30 onwards. However, no statistically significant difference occurred for adverse reactions in general in different age ranges (\(p=0.684\)).

Another important characteristic of clients in this study is that 76.6% of the sample subjects presented one or more risk factors for developing adverse reactions to the radiopaque substance, which were more frequent in people over 20 (25.6%), with a heart disease (16.0%), diabetes mellitus (11.1%) and various allergies (10.0%). Different studies\(^{[1,12]}\) indicate that the rate of adverse reactions increases about three to five times in the presence of factors like a history of previous reaction to iodinated contrast, various allergies and asthma. In this research, no significant difference was found in anaphylactoid adverse event rates with ionic iodinated contrast usage between the group with and the groups without allergic antecedents: 15.4% versus 10.2%, respectively, with \(p=0.911\).

**RADIOPAQUE MEDIUM EXTRAVASATION**

Contrast extravasation occurred in 7 of the 317 patients who received the injection through peripheral venous access, corresponding to a frequency rate of 2.2% (\(CI_{95\%}:1.0\%\);4.1%), without any relation with the type of contrast that was used. The volume of extravasated contrast ranged between 1 and 10 ml in 85.7% of cases, and only one case (14.3%) with a volume of 15 ml. All cases evolved favorably, without any complication deriving from these events.

One factor that was clearly associated with the occurrence of extravasation was the material used for the peripheral venipuncture. Usually, venous access is arranged immediately before the exam, using a 21-caliber metallic needle for manual injection and a 22-caliber plastic catheter for cases in which the radiopaque medium will be injected automatically through an injection bomb. Previously installed catheters are only used if they are in good conditions, that is, if established less than 24 to 48 hours ago, offering a good flow of 0.9% saline solution, injected in bolus to test the access; an adequate blood reflow; and no sign of phlebitis, such as pain, edema or local hyperemia. In order to avoid possible verification biases, extravasation frequency according to the type of venous access was calculated with a constant manual contrast injection technique, carried out by means of a metallic needle or plastic catheter. Extravasation rates corresponded to 10.0% in the group with metallic access, against 1.2% in the group with plastic access, indicating a significant difference in extravasation rates between the two types of intravenous devices (\(p=0.041\)).

It is equally important to compare extravasation rates according to the radiopaque substance injection technique as, in recent years, the use of the injection bomb has been related with increased occurrence levels of this adverse event in international literature. This relation is based on the fact that automatic injections administer the contrast in constant and stronger flows than manual injections\(^{[8-9]}\).

In order to analyze extravasation frequency according to the injection technique, the type of plastic venous access was maintained constant, showing extravasation in 1.2% of manual injection cases, against 1.00% when using an injection bomb. Thus, there was no statistically important difference between both techniques (\(p=1.000\)). However, it is emphasized that patients who received the automatic injection were previously assessed by the nursing team and that their venous network was considered suitable to receive the contrast agent through an injection bomb, while patients with higher risk of extravasation received a manual contrast agent injection. This may have provoked a deviation of risk cases to the manual injection group.
No significant differences in extravasation rates were found between genders and age ranges. Venous network fragility was present in 100 of the 317 sample patients, five of whom presented extravasation. This corresponds to a 5.0% extravasation rate among patients in this condition. However, the difference with the group without any risk factor was not statistically significant (p=0.101).

Literature\(^{(2, 8-10)}\) about the occurrence of extravasation refers to research that used some criteria different from those used in this study, such as the exclusive use of plastic catheters, exclusive use of automatic injection and different criteria to select the research subjects. In comparing the results of this study with international references, attempts were made to adapt results from the HCPA to the criteria used by different researchers, as shown in Table 2.

Only one international study\(^{(8)}\) presented a significantly lower percentage than results obtained at the HCPA, although extravasated contrast volumes ranged from 3 to 144 ml, with a mean volume of 41 ml. Thus, although higher rates were found in this research, extravasated volumes were significantly lower. This was fundamental for the non-occurrence of drastic consequences in the exposed patients. Moreover, other sources also mention higher extravasated volumes, ranging between 3 and 120 ml\(^{(9)}\), or do not specify the extravasated volumes\(^{(2)}\). The reduced extravasated volumes in this study, corresponding to less than 10 ml, is attributed to the fact that a nursing professional stayed at the patient’s side during the injection, identifying signs of extravasation at an early stage and interrupting the contrast flow in time to prevent more severe complications in patients exposed to this event.

Table 2 - Comparison between extravasation rates found in international publications and in this study

<table>
<thead>
<tr>
<th>Authors, year of publication</th>
<th>Criteria used in international reference</th>
<th>Extravasation in references n (%)</th>
<th>Extravasation at HCPA n (%)</th>
<th>Fisher’s Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fedite, Chang, Cordel Cagun, 1998(^{(8)})</td>
<td>Exclusive use of plastic catheter and injection bomb.</td>
<td>48.5106 (0.9)</td>
<td>2.195 (1.0)</td>
<td>p=0.707</td>
</tr>
<tr>
<td>Jacobs, Bimbaun, Langlotz, 1998 (^{(1)})</td>
<td>Does not specify catheter type.</td>
<td>41.6660 (0.6)</td>
<td>7.317 (2.2)</td>
<td>p=0.005</td>
</tr>
<tr>
<td>Bimbaun, Nelson, Cheam, Glick, 1999(^{(2)})</td>
<td>Sample subjects without risk factors for extravasation. Exclusive use of plastic catheter.</td>
<td>18.500 (3.6)</td>
<td>0.66 (0.0)</td>
<td>p=0.250</td>
</tr>
<tr>
<td>Cochran, Bomyea, Sayre, 2001(^{(3)})</td>
<td>Exclusive use of plastic catheter and injection bomb.</td>
<td>157.55571 (0.3)</td>
<td>2.195 (1.0)</td>
<td>p=0.108</td>
</tr>
</tbody>
</table>

Another study\(^{(10)}\) mentioned in table 2 tested the efficacy of an automatic accessory device linked with the contrast injection site, which detects local extravasation, automatically interrupts the injection of the radiopaque medium and does not require the health professional’s presence at the patient’s side during the injection. This research, carried out in Philadelphia, USA, presented the highest extravasation rate found in literature, with extravasated volumes ranging between 13 and 18 ml. Moreover, during the study, false-positive cases occurred in 2.4% of injections, which probably provoked the unnecessary interruption of the exam.

**FINAL CONSIDERATIONS**

When associating these research results with available international references, some divergences appeared in terms of criteria used to study adverse reactions to iodinated contrast, such as the selection of sample subjects and the signs and symptoms considered by the researcher.

As to the study subjects, the fact that this sample exclusively consists of hospitalized patients suggests a higher rate of adverse events than in studies including outpatients. Some conditions that are very common among hospitalized patients have already been associated with a two- to fourfold increase in chances for the occurrence of adverse reactions to radiopaque medium, such as exposure to surgeries, invasive procedures or regular medication intake during the five days before the exam\(^{(12)}\). With respect to immediate adverse reactions, this research considered vomiting, while international studies\(^{(1, 7)}\) exclude vomiting and include other symptoms, such as feeling hot and pain in the injection site. In other words, study results can only be compared when samples in equivalent health conditions are used and when the same research subject inclusion and exclusion criteria are adopted. However, due to the lack of information produced in conditions similar to this study context, references were used to provide parameters that could indicate the adequacy or inadequacy of local results.

In this study, immediate adverse reactions to iodinated contrast occurred at a frequency of 12.5% among patients who received ionic medium and 1.0% among patients exposed to non-ionic contrast. Intensity levels of these events were light and they were solved spontaneously. These results are within the limits quoted in literature\(^{(1, 4, 7)}\), reflecting fully acceptable and
safe rates according to international references. Consequently, it is considered that the strategy of selectively using non-ionic contrast, adopted at the service where this research was carried out, offers adequate security standards to clients, respecting the institution’s economic-financial restrictions and reflecting an adequate screening of risk cases. This demonstrates that nursing professionals have satisfactorily contributed to these results, to the extent that they actively participate in this decision process.

What contrast extravasation is concerned, this occurred in 2.2% of radiopaque substance injections through peripheral venous access, also according to parameters found in literature\(^2\text{,}8\text{-}10\). In a large majority of cases, extravasated volumes remained under 10 ml, without any complication deriving from contrast administration in the extravascular space. As to the material used to establish venous access, the use of plastic catheters revealed to be significantly safer than the use of metallic needles. International literature already mentions this significant difference in extravasation risks when using both materials, and no other research was found that used metallic needles. Thus, the use of metallic needles should be reassessed, in view of the universal use of plastic access, and new studies should be carried out to test different materials, considering the cost-benefit relation of using alternative devices.

These recommendations, based on local research data, as well as the assessment of the respective interventions, evidence the presence of improvement cycles and quality management in the health work area. Quality management has become fundamentally important in health service management, to the extent that it emphasizes continuous improvement through scientific methods and data monitoring to support decision making, with a view to achieving maximum client satisfaction and minimizing risks that can jeopardize the intended quality and security\(^\text{12}\text{-}14\). Therefore, tomography services should get to know the occurrence rates of adverse events to radiopaque medium and the conditions in which they occur, so as to obtain evidence to assess the respective care processes.

The fact that the intensity of adverse events was light and that they evolved well does not exclude the need to maintain the work team always prepared for emergency care. Severe events cannot be previewed and can occur even when non-ionic contrast agent is used, including in low risk patients, and alternative image studies that provide the same or better diagnostic information should be considered before administering iodinated contrast.

REFERENCES