

# European Society of Urogenital Radiology (ESUR) guidelines on the safe use of iodinated contrast media

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## Abstract

Since 1996 the Contrast Media Safety Committee of the European Society of Urogenital Radiology (ESUR) has released 19 guidelines regarding safety in relation to the use of radiographic, ultrasonographic as well as magnetic resonance contrast media. The committee has covered both renal and non-renal adverse events as well as other aspects of contrast media. The present paper is an overview of the work accomplished over the last 10 years regarding radiographic iodinated contrast media.

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## 1. Introduction

The first *radiographic contrast medium* to be used in clinical practice was sodium iodide, which was introduced in the 1920s. However, high toxicity and poor radiographic contrast limited the clinical use of this preparation. The breakthrough in the use of radiographic contrast media came in the 1950s with the introduction of sodium and meglumine salts of tri-iodinated benzoic acid, which are of much lower toxicity in comparison to earlier preparations but very hyperosmolar, with an osmolality 5–8 times that of the blood. The second major breakthrough came in the 1970s with the introduction of low osmolar contrast media, which was achieved by converting tri-iodinated benzoic acid into a non-ionic molecule by replacing the carboxylic acid (COOH) radical with an amide (CONH<sub>2</sub>). This molecule does not dissociate in solution providing three atoms of iodine with only one active particle [a ratio of 3:1] compared with a ratio of 1.5 [3 iodine atoms: two particles] with high osmolar contrast medium. Another development was the introduction of the mono-acid dimer in which two tri-iodinated benzoic rings are linked together with a bridge and the COOH of one ring is converted into an amide. This gives the same iodine: particle ratio of 3:1 in solution, since there are six iodine atoms and two active particles in one molecule. The osmolality of the ionic dimeric

contrast medium is almost the same as the non-ionic monomeric agents and is about twice that of the blood at iodine concentration of 300 mgI/mL. In the 1980s non-ionic dimeric contrast media were introduced; two non-ionic tri-iodinated benzoic rings were attached, giving an iodine: particle ratio of 6:1 since there are six iodine atoms and only one active particle in each molecule. The osmolality of this class of contrast media is similar to that of the blood.

Thus currently, there are four classes of contrast media available for clinical use, high osmolar ionic monomers, low osmolar non-ionic monomers, low osmolar ionic dimers and iso-osmolar non-ionic dimers. They are provided at various iodine concentrations and have different physicochemical properties (osmolality, viscosity, hydrophilicity, ions content and pH). All contrast media are distributed in the extracellular phase, they do not penetrate an intact blood–brain barrier and all are excreted via glomerular filtration. In general clinical studies have not been able to show any significant difference with regard to pharmacokinetics, pharmacodynamics, general safety, induction of thrombosis and diagnostic effect between the various non-ionic agents.

The ideal contrast agent should be totally inert causing no interactions with the organism at any level. Furthermore, the excretion should be rapid and complete. The non-ionic agents are well-tolerated by the great majority of patients. However, they are not totally inert as they are associated with a low incidence of life-threatening anaphylactoid reactions as well as moderate and minor adverse reactions. Therefore, information

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about adverse reactions including how to reduce their incidence and to treat them is of great importance. Since 1996 the committee has released 19 guidelines regarding safety in relation to the use of radiographic, ultrasonographic as well as magnetic resonance contrast media [1]. The guidelines have been well received by the radiological community not only in Europe but all over the world and are now standards for good practice at many institutions. The present paper is a short overview of the current guidelines on prevention and management of adverse reactions to iodinated contrast media, the hematological effects of these agents and their use in special clinical conditions including interaction with other drugs and clinical tests.

## 2. Adverse reactions

Adverse reactions to intravascular contrast media are not frequent and generally classified as either idiosyncratic or chemotoxic. Idiosyncratic (i.e., anaphylactoid) reactions occur unpredictably and independently of the dose or concentration of the agent. Most anaphylaxis-like reactions relate to release of active mediators. Conversely, chemotoxic-type effects relate to dose, the molecular toxicity of each agent and the physiological characteristics of the contrast agents (i.e., osmolality, viscosity, hydrophilicity, calcium-binding properties and sodium content). Chemotoxic effects of contrast media are more likely in patients who are debilitated or medically unstable. Adverse reactions can be classified into either renal or non-renal. The later may be acute (within 1 h after administration of the contrast medium) or delayed (between 1 h and 7 days after the exposure to the contrast medium). Other adverse reactions include extravasation injury.

### 2.1. Guidelines on prevention and management of acute reactions

Acute reaction to contrast media can be divided into minor, intermediate and severe life threatening reactions. The minor reactions include flushing, nausea, arm pain, pruritus, vomiting, headache and mild urticaria. Such reactions are usually mild in severity, of short duration, self-limiting and generally require no specific treatment. Intermediate reactions, more serious degrees of the above symptoms, moderate degrees of hypotension and bronchospasm. They usually respond readily to appropriate therapy. Severe life threatening reactions, these include severe manifestation of all of the symptoms included under minor and intermediate reactions, convulsions, unconsciousness, laryngeal edema, severe bronchospasm, pulmonary edema, severe cardiac dysrhythmias and arrest, cardiovascular and pulmonary collapse. The prevalence of adverse reactions with low osmolar contrast media is lower in comparison to high osmolar contrast media by a factor of five to six. Lethal reactions occur rarely.

In the era of ionic contrast media corticosteroid prophylaxis was recommended to a patient who had a history of previous generalized moderate or severe contrast medium reaction, asthma or allergy requiring medical treatment. Nowadays with the exclusive use of non-ionic contrast media in most radiology departments in the developed world opinion is divided with

regard to use of corticosteroid prophylaxis. A survey from the United Kingdom showed that 55% of responders used corticosteroid prophylaxis and 45% did not [2]. In a survey performed by the European Society of Urogenital Radiology [3] asthma was considered a significant risk factor but only 48% of the responders gave corticosteroid prophylaxis to these patients. Administration of a very short course of steroids is relatively safe and inexpensive, but should be avoided in patients with diabetes mellitus, active tuberculosis, peptic ulcer disease and in the presence of systemic infection [4,5]. Both in the United States and Europe, a wide variety of regimes with different dosages is used for giving corticosteroid prophylaxis, if it is given at all [3,6]. However, even in patients who receive both corticosteroid pre-medication and low osmolar contrast media severe adverse reactions may still occur [1,3].

The contrast media safety committee recommends that non-ionic agents should be used in patients with increased risk [(previous generalized contrast medium reaction, either moderate (e.g., urticaria, bronchospasm, moderate hypotension) or severe (e.g., convulsions, severe bronchospasm, pulmonary edema, cardiovascular collapse), asthma or allergy requiring medical treatment)] of an adverse reaction [1]. Resuscitation drugs should be available in the examination room and the patient should be observed for 20–30 min after the contrast medium injection. For extravascular applications of contrast media in high risk patients if absorption or leakage into the circulation is possible, the same precautions as for intravascular administration should be implemented.

The radiologist must be prepared to treat the acute serious adverse reactions immediately [7,8]. In patients at high risk of these reactions most radiologists avoid giving intravascular contrast media if at all possible [3]. If the examination is considered essential, non-ionic contrast media should be used, the potential risks of the procedure must be explained to the patient and the resuscitation team should be present when the contrast medium is given [3]. The vast majority of patients with severe anaphylactoid-type reactions recover if they are treated quickly and appropriately (Table 1). Most patients have reactions while they are still in the radiology department and 94–100% of severe and fatal reactions occur within 20 min of the contrast medium injection [9]. The ability to assess and treat the contrast reaction effectively is an essential skill that the radiologist should have and maintain. The first line drugs and equipment such as oxygen, adrenaline 1:1000, antihistamine H1 suitable for injection, atropine,  $\beta_2$ -agonist metered dose inhaler, I.V. fluids—normal saline or Ringers solution, anti-convulsive drugs (diazepam), sphygmomanometer and an one-way mouth “breather” apparatus should be readily available in rooms in which contrast material is injected [10]. Radiologists and their staff should review treatment protocols regularly so that each can accomplish his or her role efficiently [11–15].

### 2.2. Guidelines on late adverse reactions

Late adverse reactions to intravascular iodinated contrast media are defined as reactions occurring 1 h to 1 week after

Table 1  
Simple guidelines for first line treatment of acute reactions to contrast media

Nausea/vomiting
Transient: supportive treatment
Severe, protracted: appropriate antiemetic drugs should be considered
Urticaria
Scattered, transient: supportive treatment including observation
Scattered, protracted: appropriate H1-antihistamine intramuscularly or intravenously should be considered. Drowsiness and/or hypotension may occur
Profound: consider adrenaline 1:1000, 0.1–0.3 mL (0.1–0.3 mg) intramuscularly in adults, 0.01 mg/kg intramuscularly up to 0.3 mg max. in children. Repeat as needed
Bronchospasm
1. Oxygen by mask (6–10 L/min)
2. $\beta$ -2-Agonist metered dose inhaler (2–3 deep inhalations)
3. Adrenaline
Normal blood pressure
Intramuscular: 1:1000, 0.1–0.3 mL (0.1–0.3 mg) [use smaller dose in a patient with coronary artery disease or elderly patient]
In pediatric patients: 0.01 mg/kg up to 0.3 mg max.
Decreased blood pressure
Intramuscular: 1:1000, 0.5 mL (0.5 mg), (in pediatric patients: 0.01 mg/kg intramuscularly)
Laryngeal edema
1. Oxygen by mask (6–10 L/min)
2. Intramuscular adrenaline (1:1000), 0.5 mL (0.5 mg) for adults, repeat as needed
Hypotension
Isolated hypotension
1. Elevate patient's legs
2. Oxygen by mask (6–10 L/min)
3. Intravenous fluid: rapidly, normal saline or lactated Ringer's solution
4. If unresponsive: adrenaline: 1:1000, 0.5 mL (0.5 mg) intramuscularly, repeat as needed
Vagal reaction (hypotension and bradycardia)
1. Elevate patient's legs
2. Oxygen by mask (6–10 L/min)
3. Atropine 0.6–1.0 mg intravenously, repeat if necessary after 3–5 min, to 3 mg total (0.04 mg/kg) in adults. In pediatric patients give 0.02 mg/kg intravenously (max. 0.6 mg per dose) repeat if necessary to 2 mg total
4. Intravenous fluids: rapidly, normal saline or lactated Ringer's solution
Generalized anaphylactoid reaction
1. Call for resuscitation team
2. Suction airway as needed
3. Elevate patient's legs if hypotensive
4. Oxygen by mask (6–10 L/min)
5. Intramuscular adrenaline (1:1000), 0.5 mL (0.5 mg) in adults. Repeat as needed. In pediatric patients 0.01 mg/kg to 0.3 mg (max. dose)
6. Intravenous fluids (e.g., normal saline, lactated Ringer's)
7. H1-blocker, e.g., diphenhydramine 25–50 mg intravenously

contrast medium injection. These reactions have received increasing interest over the last decade but their prevalence remains uncertain and their pathophysiology is not fully understood [16]. The reactions include symptoms such as nausea, vomiting, headache, itching, skin rash, musculoskeletal pain and fever. A significant proportion of these reactions

are unrelated to the contrast medium. However, allergy-like skin reactions are well-documented side-effects of contrast media with an incidence of approximately 2%. Late reactions appear to be commoner after non-ionic dimers. The majority of late skin reactions after contrast medium exposure are now considered to be T-cell mediated allergic reactions. Patients at increased risk of late skin reactions are those with a history of previous contrast medium reaction and those on interleukin-2 treatment. Most skin reactions are self-limiting and resolve within a week. Management is symptomatic and similar to the management of other drug-induced skin reactions. The contrast media safety committee does not recommend prophylaxis in general but patients, who have had a previous serious late adverse reaction, can be given oral steroids [1]. One should tell patients who have had a previous contrast medium reaction or who are on interleukin-2 treatment that a late skin reaction is possible and that they should contact a doctor if they have a problem [16].

### 3. Guidelines on renal adverse reactions

The term contrast medium induced nephropathy refers to the reduction in renal function induced by contrast media. It implies impairment in renal function (*an increase in serum creatinine by more than 25% or 44  $\mu$ mol/L*) occurred within 3 days following the intravascular administration of contrast media and the absence of alternative etiology. Most authors use that definition which was endorsed by the committee in 1999 [17].

Contrast medium induced nephropathy is considered an important cause of hospital acquired renal failure [18]. This is not surprising, since diagnostic and interventional procedures requiring the use of contrast media are performed with increasing frequency. In addition, the patient population subjected to these procedures is progressively older with more co-morbid conditions [19]. Prevention of this condition is important to avoid the substantial morbidity and even mortality that can be sometime associated with contrast medium induced nephrotoxicity. Even a small decrease in renal function may greatly exacerbate morbidity that is caused by coexisting conditions [20,21]. Sepsis, bleeding, coma and respiratory failure are frequently observed in patients with acute renal failure.

The patients at highest risk for developing contrast induced acute renal failure are those with pre-existing renal impairment ( $>132 \mu\text{mol/L}$ ) particularly when the reduction in renal function is secondary to diabetic nephropathy [17,22]. Diabetes mellitus per se without renal impairment is not a risk factor [22]. The degree of renal insufficiency present before the administration of contrast media determines to a great extent the severity of contrast media nephrotoxicity. Large doses of contrast media and multiple injections within 72 h increase the risk of developing contrast medium induced nephropathy. The route of administration is also important and contrast media are less nephrotoxic when administered intravenously than when given intra-arterially in the renal arteries or in the aorta proximal to the origin of the renal blood vessels [17].

Serum creatinine is often used to determine the renal function and to identify high risk patients in spite of the limitations

of this measurement. However, serum creatinine is not an ideal marker of renal function. The serum creatinine level depends on muscle mass and is not usually raised until the glomerular filtration rate has fallen by at least 50%. Endogenous serum creatinine clearance as a measure of glomerular filtration rate is also inaccurate especially when renal function is low because of a compensatory increase in tubular secretion, which limits its validity as a glomerular filtration marker. Radionuclide techniques are preferable but each of these tests is labor-intensive and impossible to perform in all patients undergoing contrast-enhanced imaging. Alternatively, renal function can be estimated by using specially derived predictive equations. The most accurate results are obtained with the Cockcroft-Gault equation whereas the most precise formula is the Modification of Diet in Renal Disease (MDRD) study equation [23]. Unfortunately, the predictive capabilities of these formulae are suboptimal for ideal patient care. However, these methods are far superior for assessing renal function compared to a simple serum creatinine measurement. Another alternative is to use cut-off values for serum creatinine as an indicator of several levels of renal impairment. However, the use of cut-off levels (especially the low levels) will include several patients with normal renal function and use of the cut-off high levels will exclude patients with renal impairment. Despite the inaccuracies of serum creatinine measurements it is an adequate measure for identifying those patients at risk for contrast medium nephropathy as patients with normal serum creatinine ( $<132 \mu\text{mol/L}$ ) has almost no risk [22].

A questionnaire designed to elicit a history of renal disorders as well as additional risk factors for contrast media induced nephropathy (renal disease, renal surgery, proteinuria, diabetes mellitus, hypertension, gout, recent nephrotoxic drugs) may identify patients with normal serum creatinine in whom blood testing would be unnecessary [24]. The answers should be provided to the department of Radiology with the imaging request. In emergency situation serum-creatinine should always be measured if the delay of the examination does not do any harm to the patient. Before procedures requiring intra-arterial contrast medium administration serum creatinine level should always be determined. S-creatinine level must be measured within 7 days of the examination. The Department of Radiology must be informed if the serum creatinine level is increased at least 24 h before the scheduled examination time in order to make the necessary arrangements. However, a questionnaire does not completely exclude the presence of renal insufficiency, but it is practical and cost-efficient. As a matter of fact most patients referred from hospital departments have had their serum creatinine determined for other reasons within the last year and the results should be made available to the radiology department prior to contrast administration [17].

Several measures have been recommended to reduce the incidence of contrast medium induced nephropathy [24–26]. They include volume expansion, hydration with intravenous administration of normal saline solution (NaCl 0.9%) or half strength saline solution (NaCl 0.45%), infusion of sodium bicarbonate in stead of normal saline, infusion of mannitol, pharmacological manipulation (administration of atrial natriuretic peptide, loop diuretics, calcium antagonists, theophylline, dopamine,

dopamine-1 receptor antagonist fenoldopam, acetylcysteine), use of low osmolar non-ionic contrast media instead of high osmolar ionic contrast media, use of iso-osmolar contrast media instead of low osmolar contrast media, gadolinium based contrast media instead of iodine based contrast media for radiography and CT, hemodialysis rapidly after contrast administration, hemofiltration before and after contrast administration, an injection of small volume of contrast medium and avoiding short intervals (less than 48 h) between procedures requiring intravascular administration of contrast media.

Over the years various regimes of pharmacologic manipulation have been suggested in order to reduce the frequency of contrast medium induced nephropathy. The regimes have included: (1) calcium channel blockers, which prevent the influx of calcium ions through voltage-operated channels and hereby cause a vasorelaxant effect in all vascular beds including the kidney, (2) selective dopamine-1 receptor agonist (fenoldopam) which, in contrast to dopamine, increases both cortical and medullary blood flow, (3) endothelin antagonists, which play an important role in renal vasculature, (4) non-selective adenosine receptor antagonist theophylline, which also cause vascular dilatation and (5) acetylcysteine, which is an antioxidant and scavenger of oxygen free radicals. Administration of these drugs has been shown both to be effective in preventing contrast medium induced nephropathy in some studies and to be without any effect in others. Even the result of several metaanalyses has been conflicting [26]. Therefore, the contrast media safety committee does not for the time being recommend any pharmacological manipulation for routine use in prevention of contrast medium induced nephropathy.

At this moment it is unclear whether there is a difference in nephrotoxic potential between *low osmolar non-ionic monomeric* and *iso-osmolar non-ionic dimeric* contrast media. Various studies have reported conflicting results. However, it is clear that all contrast media can cause nephropathy in patients with risk factors.

Although hemodialysis can safely remove iodinated contrast media from the body it is not effective in preventing contrast nephrotoxicity [27]. The contrast media safety committee concluded that hemodialysis does not protect poorly functioning kidneys against contrast medium induced nephropathy. In addition the committee recommended that there is no need to schedule the dialysis in relation to the time of the injection of a contrast medium or the injection of the contrast agent is scheduled in relation to the dialysis program in patients on hemodialysis treatment [27]. In contrast to hemodialysis, hemofiltration was reported to be effective in reducing the incidence of this complication in patients with advanced renal impairment undergoing interventional vascular procedures [26].

Gadolinium based contrast media was recommended by some authors for radiographic examinations instead of iodinated contrast media in patients at high risk of contrast nephrotoxicity. However, this recommendation is not safe as gadolinium based contrast media are nephrotoxic particularly at doses above the ones used for MRI examinations ( $\geq 0.3 \text{ mmol/kg b.w.}$ ). In addition, gadolinium based contrast medium in approved intravenous doses up to  $0.3 \text{ mmol/kg b.w.}$  will not give diagnostic

radiographic information in most cases. Furthermore, these agents are not approved for radiographic examinations [28]. The contrast media safety committee does not recommend the use of gadolinium based contrast media for radiographic examinations to avoid nephrotoxicity in patients with renal impairment since they are more nephrotoxic than iodinated contrast media in equivalent X-ray attenuating doses [28]. However, gadolinium based contrast media might be used instead of iodinated contrast media for radiographic examinations in patients with a history of previous severe generalized adverse reaction to iodinated contrast media and in case of imminent thyroid treatment with radioactive iodine providing the renal function of the patient is not impaired [28].

Of all the above mentioned measures, extracellular volume expansion and use of low osmolar contrast media have been found to be consistently effective. Volume expansion can be achieved with the intravenous injection of at least 100 mL/h of 0.9% saline solution starting at least 6 h before contrast administration and continuing for 6–12 h afterwards [25,26]. However, this regime is not suitable for patients who are in congestive heart failure and for urgent examinations. Concurrent administration of nephrotoxic drugs such as gentamicin and non-steroid anti-inflammatory drugs should also be avoided. Mannitol and furosemide enhances the risk if nephrotoxicity and should be avoided [17].

The recently published guidelines [29–36] have not resulted in better understanding of contrast medium induced nephropathy, but caused some confusion and uncertainty. Guidelines should be based on proven clinical practice and consensus amongst experts on the subject. Guidelines should be concise, clearly written, using accurate terminology and avoiding vague recommendations. The ESUR guidelines on the prevention of contrast medium induced nephropathy [17], which required 3 years of preparation and involved wide consensus, remain valid in spite of the large number of new studies reported in the literature since its publication in 1999.

Since contrast media can induce reduction in renal function, these agents should be used with extra care in diabetic patients receiving metformin to avoid retention of metformin that may lead to lactic acidosis [38]. However, there is no conclusive evidence indicating that the intravascular use of contrast media precipitates the development of metformin induced lactic acidosis in patients with normal serum creatinine ( $<132 \mu\text{mol/L}$ ). The complication was almost always observed in non-insulin dependent diabetic patients with abnormal renal function before injection of contrast media. Therefore, serum creatinine should always be monitored before administration of contrast medium in patients receiving metformin. If the serum creatinine level is not elevated the examination can be carried out but the metformin therapy should be stopped. The administration of metformin can be resumed after 48 h providing the serum creatinine remains within the normal range. In presence of elevated serum creatinine the administration of metformin should be stopped and the injection of contrast media should be deferred for 48 h. Metformin should not be prescribed to patients with reduced renal function an alternative therapy should be considered [37].

#### **4. Guidelines on prevention and management of extravasation of contrast media**

Extravasation of contrast material is a well-recognized complication of contrast-enhanced imaging studies. The use of automated power fast flow intravenous injection in multislice CT examinations has increased its incidence of this complication and may result in extravasation of a large volume in a short period of time that may lead to severe tissue damage. Careful intravenous technique including the use of appropriate size cannula placed in a suitable vein avoiding the dorsum of the hand is recommended to avoid extravasation particularly when automated power injector is used. Fortunately, most extravasations result in no long-term sequelae. However severe skin necrosis and ulceration may occur. Large volumes ( $>50 \text{ mL}$ ) of high osmolar contrast media are known to induce significant tissue damage. Compartment syndrome may be seen associated with extravasation of large volumes. Conservative management is often adequate but in serious cases the advice of a plastic surgeon is recommended [1].

#### **5. Guidelines on the effects of contrast media on blood and endothelium**

The clinically important adverse effect of iodinated contrast media on blood and endothelium is thrombosis. High osmolar ionic contrast media may induce thrombosis due to endothelial damage, particularly in phlebographic procedures [1].

It is recognized now that all contrast media have anticoagulant properties, especially ionic agents. Drugs and interventional devices that decrease the risk of thromboembolic complications during interventional procedures minimize the importance of the effects of contrast media. The contrast media safety committee recommends that meticulous angiographic technique is mandatory and is the most important factor in reducing thromboembolic complications and that low- or iso-osmolar contrast media should be used for diagnostic and interventional angiographic procedures including phlebography [1].

#### **6. Guidelines on the use of iodinated contrast media in patients with thyroid disease**

Radiographic water soluble contrast media solutions contain small amounts of free iodide which may cause thyrotoxic crisis in patients with Graves' disease or with multinodular goiter and thyroid autonomy, especially if they are elderly and living in areas of iodine-deficiency [38]. The free iodide may also interfere with nuclear medicine diagnostic procedures and treatment for up to 2 months. Patients at risk of thyrotoxicosis should be closely monitored by endocrinologists after iodinated contrast medium injection. Prophylaxis is generally not necessary but in high risk patients particularly those in areas of dietary iodine-deficiency, prophylactic treatment may be given by an endocrinologist [38]. Intravenous cholangiographic contrast media should be avoided in patients at risk of thyrotoxicosis.

## 7. Guidelines on the use of iodinated contrast media during pregnancy or lactation

Mutagenic and teratogenic effects have not been described after administration of iodinated contrast media. Free iodide in radiographic contrast medium given to the mother has the potential to depress fetal/neonatal thyroid function. Neonatal thyroid function should be checked during the first week if iodinated contrast media have been given during pregnancy. The contrast media safety committee considers this check mandatory; however in many countries it is done routinely as part of neonatal screening [39]. Only tiny amounts of iodinated contrast medium given to a lactating mother reach the milk and only a minute proportion entering the baby's gut is absorbed. Therefore, stopping breast feeding after contrast administration is unnecessary [39].

## 8. Guidelines on the use of contrast media in patients with catecholamine-producing tumors (phaeochromocytoma and paraganglioma)

Phaeochromocytomas are relatively rare tumors, which secrete the catecholamines adrenaline and noradrenalin (epinephrine and norepinephrine). Secretion of catecholamines by phaeochromocytomas and paragangliomas may be continuous or intermittent. Typical clinical presentations include hypertension resistant to conventional treatment and intermittent crises—attacks of hypertension, headache, sweating, anxiety and pallor or flushing. Crises occur when catecholamines are released from the tumor and may be spontaneous or precipitated by drugs including contrast media or by physical compression of the tumor. The Contrast Media Safety Committee recommends that  $\alpha$  and  $\beta$ -adrenergic blockade with orally administered drugs under the supervision of the referring physician should be given before administration of intravenous contrast medium in patient with a known catecholamine-producing tumor. Before intra-arterial administration of iodinated contrast medium  $\alpha$  and  $\beta$ -adrenergic blockade with orally administered drugs and  $\alpha$ -blockade with intravenous phenoxybenzamine under the supervision of the referring physician are recommended [1]. A non-ionic agent should always be used in these patients. No special preparation is recommended in patients undergoing imaging with contrast media for incidentally detected adrenal mass [1].

## 9. Guidelines on interaction between contrast media with other drugs and clinical tests

The interactions between drugs and contrast agents are generally subdivided into: (1) drugs which will be retained in the body because of reduction in renal function induced by contrast media, (2) drugs which enhance the renal effects of contrast media, (3) drugs which enhance allergic like reactions to contrast media, (4) drugs which interfere with the hematological effects of contrast media, (5) contrast media and neuroleptic drugs, (6) drugs which enhance the effects of contrast media on the heart, (7) the effects of contrast media on isotope studies, (8) mixing contrast media with other drugs and (9) the effects of contrast media on biochemical assays [40].

The contrast media safety committee recommends that one is aware of the patient's drug history and keeps proper records of the contrast medium injection (time, dose and name). Patients taking drugs like metformin, cyclosporine, cisplatin, aminoglycosides, non-steroid anti-inflammatory drugs,  $\beta$ -blocker, interleukin-2 and hydralazine should be given special attention before injection of contrast media. In addition, contrast media should never be mixed with other drugs in tubes or syringes. Biochemical analysis of blood or urine collected within 24 h of contrast medium injection should be avoided. Measurements of clotting time and other coagulation factors can be falsely increased after the intravascular administration of iodinated contrast media, which may also interfere with determination of bilirubin, copper, iron, phosphate and proteins in blood. Contrast media in the urine may interfere with some of the protein assay techniques leading to false positive results. Contrast medium injection may interfere with some isotope studies should be avoided for at least 24 h before isotope bone scanning and before labeling red blood cells for isotope studies [40].

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