BEIJING BEILU PHARMACEUTICAL CO., LTD.

Reasonable Use of Iodine Contrast Agents and Management of Adverse Reactions

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Evaluate patient benefits/risks before use

- History of allergies: Patients who have previously experienced moderate to severe anaphylactoid reactions to iodine contrast agents or patients with a history of allergies requiring treatment are at an increased risk of allergic reactions
- Kidney function: Iodine contrast agents can cause acute kidney injury, and patients should be evaluated for related risks before surgery
- Combination medication: drugs that may increase the risk of adverse reactions to iodine contrast agents: neuroleptics and antidepressants, interleukin-2, beta blockers, metformin
- Situations where iodine contrast agents should be used with caution: lung and heart diseases, catecholamine secreting tumors, pregnant and lactating women, myeloma and paraglobulinemia, myasthenia gravis, homocystinuria
- Contraindication: uncured patients with hyperthyroidism

1. Chen Yundai and other representatives of the Expert Group on the Chinese Expert Consensus on Adverse Reactions Related to the Application of Iodine Contrast Angiography. Chinese Expert Consensus on Adverse Reactions Related to the Application of Iodine Contrast Angiography. Chinese Journal of Interventional Cardiology, 2014, 22 (6): 341 -348.
2. Chinese Society of Radiology, Chinese Medical Association, Radiologist Committee of China, Chinese Medical Doctor Association. Guidelines for the use of contrast agents (1st Edition). Chinese Journal of Radiology, 2008, 42 (3): 320-325.

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Consultation Area

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Dose limit for iodine contrast agents

- On the premise of satisfying imaging/diagnosis, the minimum dose of iodine contrast agents should be used.
- For low-risk patients, the total dose of contrast agents had better be controlled within 300 ~ 400 ml.
- Maximum dose of iodine contrast agents
  - Method I *: 5 ml ×body weight (kg)/serum creatinine (mg/dl) (not more than 300 ml) [refer to Cigarroa calculation formula]
  - Method II: 3.7 times creatinine clearance [according to 2011 ACCF/AHAUA/NSTEMI Treatment Guidelines]
- For those with severe renal insufficiency, try to choose an imaging method that does not require iodine-containing contrast agents or a non-imaging method that can provide sufficient diagnostic information.
- Avoid repeated use of the diagnostic dose of an iodine contrast agent in a short period of time. If repeated use is indeed necessary, it is recommended that the interval between two iodine contrast agent applications be ≥14 days.

* Note: The unit for detecting serum creatinine is umol/L, which needs to be converted to mg/dl. Conversion formula: 1 mg/dl = 88.4 umol/L

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Other precautions for the use of iodine contrast agents

- Preheating: Before using an iodine contrast agent, it is recommended to heat the contrast agent to 37 ℃ and place it in a thermostat.
- Hydration: It is recommended to hydrate patients within 6 to 12 hours before using an iodine contrast agent to within 24 hours after use. Hydration method: Intra-arterial drug users are advised to receive intravenous rehydration and oral rehydration concomitantly, and oral rehydration is recommended for intravenous drug users.
- Stay and observation: After the injection of a contrast agent, the patient needs to stay and be observed for 30 minutes before leaving the examination room.
- Establish an emergency channel: Establish an emergency rapid support mechanism for rescue of adverse reactions caused by iodine contrast agents with the emergency room or other clinical related departments to ensure that after an adverse reaction occurs, clinicians can promptly rush to the rescue scene for rescue if necessary.

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Iodine allergy test

- Unless otherwise specified and required in the product manual, an iodine allergy test is generally not required.
- An iodine contrast agent allergy test has no value in predicting the occurrence of allergic-like adverse reactions (patients with negative allergy test results may also develop anaphylactoid reactions or even serious anaphylactoid reactions. Conversely, patients with positive results may not necessarily develop anaphylactoid reactions). Or even the test itself can cause serious adverse reactions.

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Management of urticaria

Table 2 Treatment plan for urticaria

Type	Treatment	Dosing protocal
Mild (scattered and/or transient)	Treatment is generally not required; if symptoms are present, the following treatments may also be considered:	
	Diphenhydramine[a]	25~50mg po
	or	
	Fexofenadine[b]	180 mg po
Moderate	Monitor vital signs and maintain venous access	
(larger number and more troublesome)	Diphenhydramine[a]	25~50mg po
	or	
	Fexofenadine[b]	180 mg po
	or	
	Diphenhydramine[a]	25~50 mg, intramuscular injection or intravenous injection (intravenous injection should be slow, and completed within 1 ~ 2 min)
Severe	Monitor vital signs and maintain venous access	
(diffuse and/or progressive)	Consider diphenhydramine[a]	25~50 mg, intramuscular injection or intravenous injection (intravenous injection should be slow, and completed within 1 ~ 2 min)
	Or consider adrenaline (IM)	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection.
	or	
	Adrenaline (IV)	1: 10000 dilution, 1 ~ 3 ml intravenous injection; slowly added to the normal saline being infused

Note: a. All types can cause lassitude, and intravenous or intramuscular injection can cause or aggravate hypotension; b. the second-generation antihistamines have less effects in causing lassitude; IM: intramuscular injection; IV: intravenous injection

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Management of diffuse erythema

Table 3 Treatment plan for diffuse erythema

Type	Treatment	Dosing protocal
All types	Maintain venous access, monitor vital signs, monitor pulse oxygen saturation	
	Mask for oxygen inhalation	6~10L/min
Normal blood pressure	Generally no other treatment required	
Hypotension	Intravenous rehydration: normal saline	1000 ml, fast infusion
	or	
	Lactated Ringer's solution	1000 ml, fast infusion
If the symptoms are complicated or the fluid replacement is not effective, consider	Adrenaline (IV)[a]	1: 10000 dilution, 1~3 ml intravenous injection; slowly added to the normal saline being infused; it can be repeated once every 5~10 min, and the maximum total dose is 10 ml
	Or (if there is no venous access)	
	Adrenaline (IM)[a]	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection. The injection can be repeated, and the maximum dose is 1 mg
	Consider calling the emergency team	

Note: a. Because the perfusion of the extremities may not be sufficient to make the intramuscularly injected drug absorbed, the preferred route of administration of adrenaline in patients with hypotension is intravenous injection; IM: intramuscular injection; IV: intravenous injection

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Management of bronchospasm

Table 4 Treatment plan for bronchospasm

Type	Treatment	Dosing protocal
All types	Maintain venous access, monitor vital signs, monitor pulse oxygen saturation	
	Mask for oxygen inhalation	6~10L/min
Mild	β_2 receptor agonist aerosol (salbutamol aerosol)	2 sprays (100 μg/spray), repeatable
	Consider calling the emergency team based on the efficacy	
Moderate	Consider increasing adrenaline (IM)[a]	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection. The injection can be repeated, and the maximum dose is 1 mg
	or	
	Adrenaline (IV)[a]	1: 10000 dilution, 1 ~ 3 ml intravenous injection; slowly added to the normal saline being infused; it can be repeated once every 5 ~ 10 min, and the maximum total dose is 10 ml
	Calling the emergency team based on the efficacy	
Severe	Adrenaline (IV)[a]	1: 10000 dilution, 1 ~ 3 ml intravenous injection; slowly added to the normal saline being infused; it can be repeated once every 5 ~ 10 min, and the maximum total dose is 10 ml
	or	
	Adrenaline (IM)[a]	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection. The injection can be repeated, and the maximum dose is 1 mg
	Calling the emergency team	

Note: a. Because the perfusion of the extremities may not be sufficient to make the intramuscularly injected drug absorbed, the preferred route of administration of adrenaline in patients with hypotension is intravenous injection; IM: intramuscular injection; IV: intravenous injection

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Treatment for laryngeal edema

Table 5 Treatment plan for laryngeal edema

Type	Treatment	Dosing protocal
All types	Maintain venous access, monitor vital signs, monitor pulse oxygen saturation	
	Mask for oxygen inhalation	6~10L/min
	Adrenaline (IV)[a]	1: 10000 dilution, 1 ~ 3 ml intravenous injection; slowly added to the normal saline being infused; it can be repeated once every 5 ~ 10 min, and the maximum total dose is 1mg
	or	
	Adrenaline (IM)[a]	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection. The injection can be repeated, and the maximum dose is 1 mg
	Consider calling the emergency team based on the severity of the reaction and the efficacy	

Note: a. Because the perfusion of the extremities may not be sufficient to make the intramuscularly injected drug absorbed, the preferred route of administration of adrenaline in patients with hypotension is intravenous injection; IM: intramuscular injection; IV: intravenous injection

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Treatment for hypotension

Table 6 Treatment plan for hypotension (systolic blood pressure < 90 mmHg)

Type	Treatment	Dosing protocal
All types	Maintain venous access, monitor vital signs, monitor pulse oxygen saturation	
	Mask for oxygen inhalation	6~10L/min
	Raise the lower limbs by at least 60 °	
	Consider intravenous fluid replacement: normal saline	1000 ml, fast infusion
	or	
	Lactated Ringer's solution	1000 ml, fast infusion
Hypotension with bradycardia (pulse <60 beats/min) (vasovagal reaction)		
Mild	Generally no other treatment required	0.5 ~ 1.0 mg slow intravenous injection. Then flush the tube with saline. The administration can be repeated, and the maximum dose is 3 mg
Severe	After treatment by the above measures, if the patient still has symptoms, atropine (IV) can be used	
	Consider calling the emergency team	
Hypotension with tachycardia (pulse> 100 beats/min) (anaphylactoid reaction)		
Persistent hypotension	Adrenaline (IV)[a]	1: 10000 dilution, 1 ~ 3 ml intravenous injection; slowly added to the normal saline being infused; it can be repeated once every 5 ~ 10 min, and the maximum total dose is 1mg
	or	
	Adrenaline (IM)[a]	0.3 mg (1: 1000 dilution, 0.3 ml), intramuscular injection. The injection can be repeated, and the maximum dose is 1 mg
	Consider calling the emergency team based on the severity of the reaction and the efficacy	

Note: a. Because the perfusion of the extremities may not be sufficient to make the intramuscularly injected drug absorbed, the preferred route of administration of adrenaline in patients with hypotension is intravenous injection; IM: intramuscular injection; IV: intravenous injection

Prevention and management of vascular extravasation of iodine contrast agents

Prevention

- Choose appropriate blood vessels for venipuncture and operate carefully; when using a high-pressure syringe, choose a puncture needle and catheter that match the injection flow rate; properly fix the puncture needle; communicate with the patient and get cooperation.

Management

- Mild extravasation: Most injuries are minor and need no treatment. However, the patient should be instructed to keep observing. If the extravasation worsens, the patient should seek medical attention in time. For individuals with significant pain, common cold and hydropathic compresses can be given locally.

- Moderate and severe extravasation: ① raise the affected limb to promote blood return. ② Use 50% magnesium sulfate moisturizing cold compress in the beginning, and after 24 h change to magnesium sulfate moisturizing hot compress; or use mucopolysaccharide ointment for topical application; or use 0.05% dexamethasone for local hydropathic compress. ③ Those with severe contrast agent extravasation should be given oral dexamethasone 5 mg/time tid for 3 consecutive days on the basis of topical drug use. ④ If necessary, consult a clinician for medication.

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