Miscellaneous Pharmaceutical Agents in Interventional Radiology

Jason Oppenheimer, M.D.,¹ Charles E. Ray, Jr., M.D.,² and Kimi L. Kondo, D.O.²

ABSTRACT

Interventional radiologists employ a wide variety of drugs on a daily basis to improve patient experiences and outcomes during interventional procedures. The expectation is for the interventionalist to be well-versed in all pharmaceuticals used in the interventional suite. In this article, the authors review the following classes of common miscellaneous pharmaceutical agents used in interventional radiology: vasodilators, vasoconstrictors, antiemetics, bowel antiperistalsis agents, and prothrombotics.

KEYWORDS: Vasodilator agents, vasoconstrictor agents, antiemetics, glucagon, thrombin

Objectives: Upon completion of this article, the reader should be able to list the common interventional radiology indications, as well as complications and contraindications, for the following drug classes: vasodilators, vasoconstrictors, antiemetics, bowel antiperistaltic agents, and prothrombotics.

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The primary tools of the interventional radiologist are needles, wires, catheters, stents, and coils; nevertheless, minimally invasive procedures also require the use of adjunct pharmaceutical therapy. Without the help of common pharmaceuticals used during interventional procedures, both patient comfort and clinical outcomes would be compromised. The focus of this article is to familiarize the reader with the following drug classes: vasodilators, vasoconstrictors, antiemetics, bowel antiperistalsis agents, and prothrombotics.

VASODILATORS

Overview: Vasodilating drugs prevent or relieve arterial spasm and enhance visualization of distal arteries

through increased blood flow. This section will focus on two pharmaceuticals with different mechanisms of action used for their vasodilating effects: nitroglycerine and verapamil. A third agent (tolazoline) will not be discussed as it was withdrawn from the United States market in July of 2002.

Description and Mechanism of Action: Nitroglycerine (NG) is a short-acting vasodilator that acts by relaxing vascular smooth muscle cells. NG is converted to nitric oxide peripherally, which activates guanylate cyclase and stimulates the production of cGMP. The second messenger, cGMP, triggers a cascade, leading to the dephosphorylation of the myosin light chain and subsequent extrusion of calcium ions from the cell. The paucity of intracellular calcium relaxes the smooth

¹Northwestern University Feinberg School of Medicine, Chicago, Illinois; ²Department of Radiology, University of Colorado Denver, Aurora, Colorado.

Address for correspondence and reprint requests: Kimi L. Kondo, D.O., Assistant Professor, Department of Radiology, University of Colorado Denver, Mail Stop L954, 12401 East 17th Avenue, Room 537, Aurora, CO 80045 (e-mail: kimi.kondo@ucdenver.edu).

Pharmacology in Interventional Radiology; Guest Editors, Kimi L. Kondo, D.O. and Charles E. Ray, Jr., M.D.

Semin Intervent Radiol 2010;27:422-430. Copyright © 2010 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI: <http://dx.doi.org/10.1055/s-0030-1267854>.

ISSN 0739-9529.

muscle cell. Relaxation occurs instantaneously and lasts for several minutes depending on the dose.

Verapamil is a calcium-channel blocker that relaxes smooth muscle cells by inhibiting the influx of extracellular calcium across the cell membrane. Verapamil, a nondihydropyridine, is a less potent vasodilator than its dihydropyridine counterparts (e.g., nifedipine), and has the added effect of slowing conduction through the atrioventricular (AV) node. Verapamil exhibits peak effect within 5 minutes and actions last 10 to 20 minutes.

Preparation, Administration, Dosage, and Method: Depending on the site, between 50 and 300 μg of 10 $\mu\text{g}/\text{mL}$ NG solution is administered as an intravascular bolus. Polycarbonate or glass syringes should be used to administer NG as the agent adheres to conventional polyvinylchloride plastic syringes. Care should be taken to not expose NG to light. Alternatively, NG can be administered as a paste, which is applied topically to the skin over the area of interest. A sheet of paper can be used to spread the paste (while wearing gloves at all times).

Verapamil can also be administered intraarterially as a bolus of 1 to 10 mg, usually in a dilution of 10 mL of saline.

With all vasodilators, the blood pressure of the patient should be monitored closely following drug administration.¹⁻⁵

Indications: NG is a short-acting, safe, effective vasodilator, making it the favored agent for many interventionalists in the prevention and treatment of catheter-induced vasospasm. In addition, NG can be used to dilate distal vascular beds when measuring pressure gradients across a stenotic lesion.

Verapamil is an alternative to NG in the prevention and treatment of vasospasm. Verapamil is considered a more potent, longer-acting vasodilator than NG. It is gaining favor in mesenteric angiography, and is the preferred agent for the treatment of cerebral arterial spasm.³⁻⁵

Complications and Contraindications: Adverse reactions are uncommon when vasodilators are used at the standard interventional doses. As a class, vasodilators share many common adverse reactions: systemic hypotension (especially in patients taking phosphodiesterase inhibitors for impotence), headache, tachycardia, and nausea/vomiting. Vasodilators are contraindicated in patients with prior hypersensitivity reactions, elevated intracranial pressure, constrictive pericarditis, or pericardial tamponade. Verapamil should not be used in patients with cardiac conduction abnormalities. If adverse reactions occur, the vital signs of the patient should be monitored closely, and IV fluids given as necessary. To improve cerebral perfusion, the legs can be elevated and the patient may be placed into the Trendelenburg position.^{1,3}

VASOCONSTRICTORS

Vasopressin

Overview: Vasopressin, a potent vasoconstrictor, is useful in the setting of acute gastrointestinal bleeding.

Description and Mechanism of Action: Vasopressin is an exogenous form of the naturally occurring pituitary peptide, antidiuretic hormone (ADH). Vasopressin exerts a vasoconstrictor effect through presumed cAMP mechanisms and promotes the contraction of vascular smooth muscle. These effects are specific to capillaries, small arterioles, and small venules. Degradation of vasopressin occurs in the liver and kidneys. The half-life of vasopressin in plasma is 10 to 20 minutes.¹⁻³

Preparation, Administration, Dosage, and Method: Vasopressin is administered via an intraarterial infusion with the catheter positioned selectively within the main trunk of the target artery (usually the superior mesenteric artery or the inferior mesenteric artery). The initial dose is usually 0.2 U/min. Repeat arteriograms are performed to assess for bleeding or vasoconstriction and the dose titrated accordingly. Doses above 0.4 U/min are not beneficial and if the bleeding is still not controlled then alternatives, such as embolization or surgery, should be considered. Once bleeding is controlled, the infusion is continued for 12 to 24 hours, while tapering the dose by half every 6 to 12 hours if there is no further bleeding. When the continuous infusion rate reaches 0.1 U/min for 6–12 hours, the infusion is switched to normal saline; the catheter can be removed after 4 to 6 hours of no bleeding with normal saline infusion.^{3,4}

Indications: For over 40 years, vasopressin has been employed to control gastrointestinal bleeding. Nusbaum et al described the first case of intravascular vasopressin infusion to control variceal bleeding in 1968⁶; arterial gastrointestinal bleeding applications quickly followed suit.⁷ In the 1990s, embolization replaced the use of vasopressin for upper GI bleeds, however vasopressin was still preferred for lower GI bleeds because of its high efficacy and high rates of bowel infarction after embolization procedures.⁸ With the advent of new microcatheters and new embolization agents, embolization is now considered a primary option in the treatment of both upper and lower GI bleeds.⁹

Today, vasopressin infusion is preferable in cases where embolization is technically not feasible or contraindicated, such as diffuse mucosal bleeding (e.g., inflammatory processes such as gastritis or granulomatous disease). Additionally, vasopressin may be used when embolization procedures are contraindicated. Vasopressin infusion requires less time finding the correct target and less skill directing catheters through difficult routes into small, tortuous, spasm-prone arteries. However, rebleeding is common when using vasopressin and occurs in ~20% of cases.¹⁰ The vasoconstrictive effects of the drug disappear once the infusion stops and

prevention of rebleeding is reliant on clot formation and retention. Another common cause of vasopressin failure is due to atherosclerosis because such arteries do not vasoconstrict in response to vasopressin.

Even with recent advances in embolization technology, vasopressin remains a safe and effective choice in lower GI bleeds. Vasopressin infusion is greater than 90% effective in controlling lower GI diverticular bleeding,¹⁰ and success rates for all etiologies of lower GI bleed range up to 90%.¹¹⁻¹³

Complications and Contraindications: Complications of vasopressin infusion include cardiovascular and ischemic complications. Common adverse reactions include headache, diaphoresis, nausea/vomiting, and abdominal cramps. Antidiuretic effects (e.g., decreased urine output, electrolyte instability, and hypertension) can manifest hours after infusion. Hypertension, arrhythmias, and myocardial infarction occur in less than 5% of cases. Bowel infarction and peripheral vascular ischemia occur in less than 1% of cases.¹⁴ Extreme care should be exercised when administering vasopressin to patients with coronary artery or peripheral vascular disease because vasopressin can precipitate angina or myocardial infarction. Because vasopressin increases extracellular fluid levels, additional caution should be used in patients with cardiac, renal, or hepatic failure.^{1,3}

Epinephrine

Overview: Epinephrine, a nonspecific adrenergic agonist, at one time was used frequently in interventional radiology for its vasoconstricting properties in renal and mesenteric arteriography.^{4,15,16} Epinephrine-assisted angiography has largely been replaced as digital subtraction angiography, balloon occlusion catheters, and better computed tomography (CT)/magnetic resonance imaging (MRI) classifications easily define renal masses. At this point, intraarterial epinephrine has little place in the interventional suite, except for its uses in contrast reactions and cardiopulmonary resuscitation.

ANTIEMETICS

Overview: Several pharmaceuticals exist for the treatment of nausea and vomiting. As interventional radiologists find more applications in oncologic and palliative settings, increased importance is placed on understanding these drugs. Furthermore, nausea and vomiting often are a component of postembolization syndrome, a common phenomenon experienced in patients undergoing solid organ embolization. This section will provide an overview and explore the use of ondansetron, promethazine, and scopolamine in interventional settings.

Description and Mechanism of Action: Ondansetron (Zofran[®], GlaxoSmithKline, Brentford, London, UK) is a selective serotonin antagonist specific to the 5HT₃

receptor, which is found both peripherally in the intestines and centrally near the vomiting center. The exact antiemetic properties of ondansetron are unknown.

Promethazine (Phenergan[®], Wyeth Pharmaceuticals, Collegeville, PA) is a phenothiazine with little neuroleptic potential used primarily for its antihistamine (H₁) blocking properties. The antiemetic and antimotion properties are thought to be due to a combination of blocking histamine in the gut and anticholinergic activities in the medulla oblongata.

Scopolamine, like atropine, antagonizes acetylcholine at the muscarinic receptor. Scopolamine is thought to interfere with vestibular pathways from the inner ear to the brainstem, making it useful for the treatment of nausea/vomiting induced by motion sickness.

All three drugs are extensively metabolized by the liver and must be dose-adjusted in patients with hepatic impairment. Both ondansetron and promethazine rely on CYP450 hepatic enzymes for degradation, and are affected by inducers and inhibitors of this system.^{1,2}

Preparation, Administration, Dosage, and Method: Ondansetron is commonly given in oral or IV form. For postprocedure prophylaxis in adults (including the elderly), a single 16 mg oral dose one hour prior to the procedure or 4 mg IV immediately prior to anesthesia is recommended. For chemo- and radiotherapy prophylaxis in adults, an 8 mg oral dose 30 minutes prior to the procedure followed by 4- and 8-hour doses postprocedure is recommended. Alternatively, a single IV dose of 4 mg starting 30 minutes prior to the procedure can be used. Therapy can be continued every 8 hours as needed.

Although the preferred method of administration of promethazine is orally, it is typically given IV in the interventional suite. A single dose of 6.25 to 12.5 mg IV is given, and can be repeated every 6 hours. Promethazine has a significant sedative side effect.

Scopolamine is easily given by transdermal patch (1 mg/day). The patch gives ideal results when placed to the skin behind the ear 4 hours prior to the procedure. The effect lasts up to 3 days. If a repeat dose is needed, a second patch is typically placed behind the opposite ear.^{1,17}

Indications: With its many chemotherapy/radiotherapy and surgical applications, ondansetron naturally fits within the arsenal of the interventional radiologist. Originally approved for chemotherapy-induced vomiting in 1991, ondansetron quickly gained approval for postsurgical vomiting in 1999. Ondansetron is both more effective than traditional antiemetics and extremely safe. Ondansetron prophylaxis is now common practice prior to interventional procedures with patients at high risk for nausea/vomiting; these include most embolization procedures, especially when chemotherapy or radiation is involved.¹⁷ Additionally, ondansetron can successfully treat pruritus secondary to cholestasis.¹⁸

Promethazine is used in place of ondansetron for nausea/vomiting when sedating effects are deemed beneficial to the patient. In addition to its antiemetic effects, promethazine is often used as an adjunct to analgesics during periprocedural sedation. As such, promethazine is often administered to patients to induce a "quiet" sleep to ease apprehension before a procedure.

A scopolamine patch is more effective for nausea and vomiting induced by motion. Its ease of administration makes scopolamine the antiemetic of postprocedure choice in many interventional suites.

Complications and Contraindications: Ondansetron is extremely well tolerated, with headache and diarrhea being the most common adverse reactions. Ondansetron should be used with care in patients with extensive hepatic disease; no more than 8 mg/day should be given to patients with poor liver function. Electrocardiogram changes and sudden blindness are rare complications following IV administration.^{19,20} Pregnancy class B, ondansetron is safely used during pregnancy and, in fact, is a first-line treatment for hyperemesis gravidarum.²¹ Ondansetron is excreted in breast milk and should be used cautiously in women who are breastfeeding.

Promethazine is associated with numerous side effects, but because of the low dose and brief administration used in interventional procedures it is generally tolerated well. Most commonly, patients on promethazine experience anticholinergic side effects; special care should be taken in patients on psychiatric or antiseizure medications. At high doses over an extended period, extrapyramidal symptoms, neuroleptic malignant syndrome, and tardive dyskinesia are reported with promethazine administration. The most common extrapyramidal symptom experienced is akathisia, which can be counteracted by concomitant administration of diphenhydramine. Importantly for the interventionalist, promethazine interferes with the vasopressor effects of epinephrine. Promethazine is pregnancy class C and is not recommended when breastfeeding for risk of seizure in the infant.¹

Scopolamine is well tolerated, with anticholinergic symptoms being the most common side effects. Specifically, dry mouth is experienced by up to two-thirds of patients on the patch. As with any medication with anticholinergic properties, care should be taken in patients with glaucoma, prostatic hypertrophy, and bowel obstruction. Because of its atropine-like qualities, scopolamine is relatively contraindicated in patients with chronic obstructive pulmonary disease, myasthenia gravis, coronary artery disease, congestive heart failure, and dysrhythmias. A scopolamine patch should be removed prior to MRI examinations, as aluminum in the packaging can cause burns. Scopolamine is pregnancy class B and can be used in women who are breastfeeding.²²

BOWEL ANTIPERISTALSIS AGENTS

Overview: Glucagon, through the inhibition of gastrointestinal (GI) motility, both optimizes radiographic visualization and procedures involving the GI tract by reducing bowel tone/spasm and increasing the comfort of the patient.^{23,24}

Description and Mechanism of Action: Recombinant glucagon is synthesized by yeast or bacteria in identical structure and function to the natural pancreatic peptide. The mechanism by which glucagon relaxes the smooth muscle of the GI tract is unknown. Degradation of glucagon occurs in the liver and kidneys.^{1,3}

Preparation, Administration, Dosage, and Method: Glucagon must be given intramuscularly (IM) or IV because the peptide is completely degraded by GI enzymes. Glucagon is supplied in lyophilized form and is reconstituted with 1 mL of sterile water (1 mg/mL), and the preparation should be used immediately.

The recommended dose of glucagon is dependent on the desired onset, duration, and location of relaxation. Onset is generally rapid (~1 minute for IV, ~5 minutes for IM) and lasts for 10 to 30 minutes. A dose of 0.25 to 2 mg IV or 1 to 2 mg IM is recommended.

Certain regions of the GI tract are more resistant to the action of glucagon and require higher doses for relaxation. For optimum results, the colon requires a 2 mg IM dose 10 minutes prior to a procedure. The stomach requires 0.5 mg IV or 2 mg IM of glucagon. Most sensitive, the small bowel only requires 0.25 mg IV or 1 mg IM.^{1,25,26}

Indications: Radiologists made the switch from anticholinergic agents to glucagon for bowel hypotonia in the early 1970s. Since this time, radiologists have used glucagon to stabilize the GI tract in barium and MRI studies.

The main indication for glucagon in the interventional suite is to decrease bowel peristalsis during digital subtraction arteriography in abdominal vascular procedures. Glucagon is especially helpful in the context of a GI bleed where bowel immobility is a crucial aspect of localizing the lesion. Glucagon can also facilitate many other abdominal procedures: biopsies, abscess drainage, esophageal or colonic stenting, and gastrostomy tube placement.²³⁻²⁶ For feeding tube placement, glucagon helps to decrease pyloric opening. This traps gas in the stomach, facilitating gastrostomy tube placement. However, glucagon should not be used during gastrojejunostomy tube placement for the same reason because it will hinder the ability to place a wire or catheter beyond the pylorus.

Complications and Contraindications: Interventional procedures use small doses of glucagon that are usually well tolerated. Nausea/vomiting, the most frequent adverse reaction experienced, is dose dependent and can be curbed by slow IV injection over one minute. Glucagon is contraindicated in patients with known

hypersensitivity reactions, as well as in patients with pheochromocytoma, because it stimulates the release of catecholamines. In addition, glucagon should be used with caution in patients with cardiac or coronary artery disease as the drug is a known cardiac stimulant. Reports of reflexive hypoglycemia up to several hours postprocedure exist, and all patients receiving glucagon should be monitored for signs of lightheadedness, dizziness, or headache. Due to the low doses used and B pregnancy classification, glucagon should not cause problems in pregnant women or women who are breastfeeding.²⁵

PROTHROMBOTICS

Thrombin

Overview: Thrombin, a naturally occurring protein, is a crucial component of the clotting cascade. Approved by the Food and Drug Administration (FDA) in 1944, thrombin gained popularity in the field of interventional radiology for the off-label use of treating postcatheterization pseudoaneurysms (PSA) in the late 1980s. The high success rate and noninvasive nature of percutaneous image-guided PSA repair has led to the use of thrombin for treating various aneurysm types in vessels throughout the body, including sealing type II endoleaks. Topical thrombin (D-stat[®]) will be discussed later.

Description and Mechanism of Action: Thrombin, a serine protease whose precursor is synthesized by hepatocytes, forms clot by converting soluble fibrinogen into insoluble fibrin. The clot forms within seconds and is directly related to the concentration of thrombin. The clinical application of thrombin is to accelerate the natural clotting process. When used correctly, thrombin is considered to be safer than other thrombotic or embolic agents because blood vessels have natural defense mechanisms to break it down; the clot that escapes downstream may be rapidly degraded by circulating plasmin and tissue plasminogen activator released by endothelial cells in response to anoxia.

Currently, two forms of thrombin are available in the U.S. market: bovine and human. Bovine thrombin is time-tested, cheap, and poses fewer personnel or religious barriers than its counterpart. The main advantage of human recombinant over bovine thrombin is the lower dose needed to accomplish thrombosis. Human recombinant thrombin additionally poses less risk for allergic reactions and prion contamination.¹⁻³

Preparation, Administration, Dosage, and Method: Thrombin is packaged as a powder and must be reconstituted with sterile normal saline immediately prior to injection. Although many different concentrations and dosages have been described and recommended, these values are highly dependent on the size and location of the injection site. A thrombin concentration of 1000 IU/mL is standard practice; however, concentrations as low

as 100 IU/mL are proven to have no decrease in efficacy. Usually between 0.3 and 3 mL (300–3000 IU) of thrombin is necessary for complete thrombosis.

Thrombin is administered using sterile technique under image-guidance, usually ultrasound or CT (see Fig. 1). A 19- to 25-gauge needle is advanced into the center of the target; thrombin is slowly injected at a constant rate until the hypoechoic PSA turns to hyperechoic clot and intraluminal blood flow ceases, as demonstrated by color Doppler ultrasound. Most authors agree that slow administration over 10 seconds or more is advised. Complete occlusion is usually accomplished within seconds, but additional injections may be attempted if the first is unsuccessful or if recanalization occurs. Because thrombin administration works by initiating the clotting cascade, injection should stop as soon as clot formation is visualized on duplex ultrasound.^{1-3,27,28}

Indications: The most common use of intravascular thrombin is for PSA repair in peripheral vessels, where the goal is to thrombose the false sac to prevent future rupture and to decrease the risk of distal embolization. The first description of percutaneous injection of thrombin to repair postcatheterization PSA was reported by Cope and Zeit in 1986.²⁹ The authors demonstrated that the administration of thrombin for intraaneurysmal repair was safe and effective by presenting four cases: three PSA repairs involved the femoral, iliac, and peroneal arteries, and one true aneurysm repair of an accessory hepatic artery was performed. In subsequent years, several case series redemonstrated the safety, speed, efficacy, and painless nature of thrombin injection in PSA repair.³⁰⁻³³ Reported overall technical success rates (thrombosis) are as high as 95 to 100%.^{28,34} Although arteries of the extremities are common locations of postcatheterization PSA formation, successful repair of lumbar³⁵ and crural³⁶ artery PSAs have also been reported.

Image-guided percutaneous thrombin injection has largely replaced ultrasound-guided compression as the treatment for postcatheterization PSAs.³⁷ Comparison studies between percutaneous thrombin injection and ultrasound-guided compression in the treatment of PSAs all demonstrate thrombin injection to be superior in both success and speed.³⁷⁻³⁹ In the only prospective randomized control trial between thrombin and ultrasound-guided compression in femoral PSA repair, at 24 hours thrombosis was achieved in 100% (15/15) of patients treated with thrombin compared with only 13% (2/15) in the compression group.³⁷ No complications occurred in either group.

Due to its success in treating PSAs in peripheral vessels,^{28,32,34,37} thrombin has also been used to treat visceral PSAs. Postpancreatitis PSAs can occur in the splenic, gastroduodenal, pancreaticoduodenal, gastric, hepatic, and superior mesenteric arteries. Thrombin

Figure 1 Pseudoaneurysm repair using intraarterial thrombin. (A) Color Doppler ultrasound image demonstrating a typical appearance of a femoral pseudoaneurysm (2.55 cm $\times$ 2.08 cm) commonly referred to as the “yin-yang” sign. Also demonstrated is the pseudoaneurysm neck and the communication with the left femoral artery. (B) Doppler tracing of the center of the pseudoaneurysm demonstrating the mixture of forward and backward blood flow. (C) Pseudoaneurysm postadministration of 200 U of intraarterial thrombin using a 25-gauge needle, which demonstrates thrombus and no blood flow within the pseudoaneurysm.

treatment has been reported for this indication by several authors.^{40–42} Although pancreatitis is the most common cause of visceral PSAs, idiopathic PSAs can develop in multiple locations. Successful splenic,⁴³ superior mesenteric,⁴⁴ and pulmonary artery⁴⁵ PSA repairs have been reported, and even one case of thrombin treatment of a left ventricular PSA is described.⁴⁶ In addition, thrombin injection has been shown to be a reasonable alternative for the treatment of visceral mycotic aneurysms.⁴⁷

Less common uses of thrombin include its use in the repair of true aneurysms and endoleaks. True aneurysms of the splenic artery⁴³ are reported to be amenable to thrombin injection alone; however, in other arterial locations its role is mainly as an adjunct to embolic coils.²⁷ When used as an adjunct, coils may be soaked in thrombin to facilitate vessel thrombosis. In true aneurysms, thrombin must be injected very slowly to assure no injection into the systemic circulation. Repair of type II endoleaks with thrombin injection is associated with low morbidity.^{48,49}

Complications and Contraindications: Complication rates of thrombin injection are low (<4%),^{27,34,50} but can be serious and dictate careful patient selection. Downstream thromboembolic events are the highest reported serious complication (0.8%)³³; patient pulses and ankle-brachial indexes must be recorded prior to the

procedure. Thrombin injections should not be performed in any patient with local infection, and distal ischemia is a relative contraindication.

To ensure success, all PSAs should be carefully evaluated with ultrasound prior to injection to evaluate the relevant anatomy: size of the sac and neck, adjacent vessels, and existence of arteriovenous fistulas or septations. Large aneurysm neck size (>10 mm) is associated with increased risk of distal embolus or thrombosis. During thrombin administration, an attempt should be made to keep the needle tip away from the neck to prevent escape of clot into the distal systemic circulation. Some authors recommend balloon occlusion of the PSA neck; however, this approach adds time in the IR suite and an invasive procedure with associated risk. Some authors recommend using lower concentrations of thrombin (100 IU/mL),⁵¹ but this practice needs validation through further investigation.

Method aside, patients should receive immediate and 24-hour postprocedural follow-up where peripheral pulses, ankle brachial index, and/or imaging can be used to assess for complication and recanalization of the PSA. In the event of distal nontarget occlusion, prompt intra-arterial thrombolysis should be performed.^{27,28,34,51} In the event of recanalization (2% of cases), a second attempt can be made; however, lower success rates are noted with such repeat procedures.³³ If deemed

necessary, ultrasound follow-up 7 to 10 days later can assure PSA thrombosis.

Other complications of intravascular thrombin injection include PSA rupture as well as injection site (e.g., cellulitis and groin abscess) and hypersensitivity (e.g., fever, urticaria, and anaphylaxis) reactions. Patients should be asked if they have allergies to thrombin or preexposure to thrombin, as bovine thrombin is highly immunogenic. If hypersensitivity is suspected, skin-prick testing can be performed, or human recombinant thrombin can be used in place of bovine thrombin.^{28,34,52} A postinjection transient fever is described in several patients and is thought to be a form of mild allergic reaction. Fever is not a cause for immediate concern, but should be recorded and reconsidered during future thrombin administration.

Limited data exist regarding thrombin use in children and pregnant women. Successful accounts are reported in children, but the small size of the arteries make ischemic complication more likely.^{53,54} Thrombin is pregnancy risk class C and should be given when benefits outweigh the risks. There is no contraindication in women who are breastfeeding.

Topical Thrombin

Overview: Topical thrombin aids in the control of surface bleeding after intraarterial puncture, percutaneous biopsy, or dialysis access procedures.

Description and Mechanism of Action: See discussion earlier.

Preparation, Administration, Dosage, and Method: Topical thrombin usually comes in a sterile kit. A

common topical thrombin used is D-stat[®] (Vascular Solutions Inc., Minneapolis, MN), which is available in dry wrap and flowable forms.

The dry wrap package contains a lyophilized pad within gauze containing 200 IU of bovine thrombin, calcium chloride (an inducer of the clotting cascade), and sodium carboxyl methylcellulose (a matrix for clot formation). The pad is placed over areas of surface bleeding and pressure is applied. Pressure is gradually reduced until hemostasis is achieved. The pad may be removed or left in place for a few hours. The treatment site should remain dry. Care should be taken when removing the pad as to not dislodge the clot; if the pad becomes stuck, gentle irrigation using normal saline can be helpful.

D-stat[®] flowable is a similar product mixed into a thick solution that can be applied into sites of surface bleeding with a syringe-like device.^{1,27,55}

Indications: Topical thrombin is becoming increasingly popular for its hemostatic properties after interventional procedures. Many patients undergoing procedures in the interventional suite have underlying platelet dysfunction or coagulopathies, and cessation of surface bleeding is difficult to achieve. Topical thrombin is useful in controlling puncture site bleeding after angiography, catheter placement, and percutaneous biopsies. In addition, topical thrombin helps manage bleeding after dialysis access procedures such as tunneled catheter placement or cannulation of an AV fistula.

Complications and Contraindications: Topical thrombin is safe and well-tolerated. When applying thrombin, care should be taken to not introduce any drug intraarterially as complications discussed in the

Table 1 Pitfalls and Pearls for Miscellaneous Drugs

Vasodilators	<ul style="list-style-type: none"> • If nitroglycerine is not to be given immediately after drawing up the solution, use polycarbonate or glass syringes as the agent adheres to conventional polyvinylchloride plastic syringes. • Remember to wear gloves and spread nitropaste with paper.
Vasoconstrictors	<ul style="list-style-type: none"> • Consider vasopressin infusion when treating diffuse mucosal bleeding (e.g., gastritis). • Rebleeding occurs in ~20% of patients following intraarterial vasopressin infusion. • Vasopressin can precipitate angina or myocardial infarction.
Antiemetics	<ul style="list-style-type: none"> • Remove scopolamine patches prior to MRI to prevent burns. • Ondansetron can successfully treat pruritus secondary to cholestasis. • Diphenhydramine, when given concurrently, prevents feelings of restlessness and increases the sedative properties of promethazine.
Bowel antiperistaltic agents	<ul style="list-style-type: none"> • Glucagon, by decreasing the pyloric opening, helps gastrostomy tube placement by trapping gas in the stomach, but hinders the ability to place a wire or catheter beyond the pylorus in gastrojejunostomy tube placement. • The colon requires more glucagon than the stomach or small bowel for relaxation.
Prothrombotics	<ul style="list-style-type: none"> • Because thrombin works by initiating the clotting cascade, the injection should stop as soon as clot formation is noticed on duplex ultrasound. • During thrombin administration, keep the needle tip away from the PSA neck to prevent escape of clot into the distal systemic circulation. • Consider the use of topical thrombin in difficult-to-control surface bleeding.

MRI, magnetic resonance imaging; PSA, postcatheterization pseudoaneurysms.

previous thrombin sections can occur. Contraindications exist for patients allergic to bovine products.

CONCLUSION

Miscellaneous pharmaceuticals are helpful adjuncts for diagnostic and therapeutic procedures in interventional radiology when used for the appropriate indication in the proper patient populations. Familiarity with these medications, and potential complications with their use, is essential for any individual using them in the interventional radiology suite. Common pitfalls and pearls regarding these medications are summarized in Table 1.

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