

Agents Used in Treatment of Vascular Malformations

Introduction:

- Diagnose vascular anomalies by clinical exam and MRI, not by diagnostic angiography.
- If you need to do a diagnostic angiogram, image the venous phase.
- Check coagulation parameters on patients with large VMs.
- Anticoagulation for two weeks helps reverse consumption coagulopathy.
- Never use ethanol in the orbit.
- Never use sodium tetradecyl intra-arterially.
- Never coil a proximal feeding artery.

Classification of Vascular Anomalies

Vascular anomalies are divided into two groups:

- A. Tumors e.g. hemangiomas
- B. Vascular malformations.

Malformations are categorized according to channel type and flow characteristics. High-flow vascular anomalies include arteriovenous fistula (AVF) and arteriovenous malformations (AVM).

Low-flow malformations include capillary malformations (CM), venous malformations (VM) and lymphatic (LM) malformations.

Some patients have combined channel anomalies (e.g. Klippel–Trenaunay syndrome (CLVM)).

Techniques

Endovascular techniques for treating vascular malformations consist predominately of embolisation and sclerotherapy. Arterial embolisation is reserved for high-flow vascular malformations.

Embolisation Agents

1. Polyvinyl Alcohol Foam Particles (PVA)

Polyvinyl alcohol was first utilised in foam form in the early 1970's. Currently, the material is available as particles ranging in size from approximately 50 microns to 2,000 microns. As such, the level of embolisation can be tailored to the clinical scenario at hand. As with other very small particulate agents, the smallest size of PVA may result in significant tissue ischemia and should be reserved mostly for tumor embolisation. PVA is delivered through the catheter in suspension form. The particles are mixed in a combination of saline and contrast either in a bowl or in syringes with mixing occurring across a three-way stop cock. PVA has a tendency to flocculate or settle out of solution. Immediately prior to injection, the material should be resuspended so that uniform injection can be obtained. Non-uniform delivery of the material can result in occlusion of the delivery catheter. Aggregation of PVA may result in a more proximal occlusion than intended.

PVA causes direct mechanical obstruction and induces a foreign body type reaction with permeation of the particles by granulation tissue. Over time this reaction subsides and months to years later, the vessel may recanalise. Although PVA is considered to be a permanent agent, it will recanalise over time.

PVA is utilised predominantly for tumor embolisation as well as pre-operative devascularisation of other lesions. PVA is the preferred embolic agent for bronchial artery embolisation and the 500-700 micron diameter particles are utilised extensively for fibroid embolisation.

Mechanism of Action: cause occlusion of the vascular bed and obstructs inflow.

2. Embospheres

Embosphere particles are a new addition to the list of approved materials for arterial embolisation. These particles are hydrophilic, acrylic based spheres. Available sizes are similar to PVA and they come in sterile vials, which are easy to use. EmboGold particles are a highly visible form, which comes in sterile prefilled syringes.

Advantages of these particles are their compressibility. Less catheter clogging leads to less catheter exchanges due to occlusion. Better penetration of particles into the vascular bed allows for a more uniform embolisation. They have been extremely well received for uterine fibroid embolisation.

A disadvantage may be a slightly higher per vial cost. The end-point for embolisation is somewhat different than with PVA.

3. Gelfoam

Absorbable and should not be used in AVM's.

Mechanism of Action: cause a combination of vascular thrombosis and endothelial ablation, resulting in fibrosis.

4. NBCA – Histoacryl (Glue)

Cyanoacrylate materials have been used as adhesive embolic agents for more than 20 years. Their role in the embolisation of high-flow vascular lesions has been well established. Indications of NBCA are numerous, including the embolisation of various types of cerebral and spinal vascular malformations, as well as a growing number of peripheral vascular lesions, such as systemic AVMs.

Mechanism of Action: The obliteration of a blood vessel embolised with a cyanoacrylate agent results from a polymerization process induced by the contact of the glue with an ionic environment such as blood or normal saline. Hence the importance of flushing the delivery microcatheter with dextrose 5%, a nonionic solution, prior to NBCA injection. In addition to their immediate mechanical effect, cyanoacrylate agents also induce a chronic inflammatory response, which is believed to play an important role in the permanency of the occlusion obtained with NBCA. This response can range from a mild histiocytic reaction confined to the vessel lumen, sparing the vessel walls or contiguous parenchymal tissues to more intense inflammatory reactions, including the occurrence of patchy mural angioneclerosis. The permanency of the vascular obliteration obtained with cyanoacrylate agents depends in part to the homogeneity of the glue cast. In other words, it is preferable to obtain a continuous NBCA column rather than a mélange of glue and trapped blood that potentially opens the door to recanalization processes. When treating vascular lesions characterized by the presence of arteriovenous shunts, such as arteriovenous malformations or fistulas, it is necessary for the glue to reach the actual shunt site rather than just sit more proximally in the arterial feeders.

5. Onyx™ Liquid Embolic System

Ethylene-vinyl alcohol copolymer or EVOH consists of a polymer mixed with tantalum in a dimethyl sulfoxide (DMSO) base. This material can be injected through a catheter and once it comes into contact with the bloodstream, the DMSO diffuses out of the solution allowing the EVOH polymer to precipitate creating a cast of the vessel with direct mechanical occlusion. The operational principles are similar to using glue. With the current agent, it is difficult to predict the exact depth of penetration and the time to polymerization. One significant advantage when compared to glue is that this is not an adhesive agent and there is no risk of gluing the catheter in place.

Mechanism of Action: cause occlusion of the vascular bed and obstructs inflow.

6. Coils.

Coils should rarely be used in mid to low flow AVM's as it will not occlude the nidus and prevent the interventionalist from getting to the AVM nidus at a later stage. Coils can be beneficial in high flow AVM's or AVF's.

Coils are available in almost all sizes from approximately 2 - 30 mm in diameter and are constructed of both stainless steel and platinum. Dacron fibres are woven into the coil to increase the thrombogenicity of the coil. In addition to direct mechanical occlusion by the coil, the Dacron fibers act as a nidus for thrombus formation. Extensive inflammatory changes are induced in the occluded arteries as well as in the periadventitial tissue. Coils produce a permanent focal occlusion leaving the vessel distal to the coils patent. The use of coils is analogous to a focal surgical ligature of the vessel.

The size of the desired coil should be matched to the size of the vessel. If the coil is smaller than the vessel, the coil may embolise too far distally or through an AV fistula. Alternatively, if the coil is oversized, the coil may cause recoil of the delivery catheter with subsequent reflux of the coil back into the parent vessel.

Platinum/Fiber coils are MRI compatible.

7. Balloons

Detachable balloons have recently been reapproved for vascular use and are extremely efficacious for high flow arterial venous fistulas. Balloons cause mechanical occlusion of the vessel with formation of thrombus proximal and distal to the balloon. Advantages include precise deployment and retrievability. Although the current balloons are made of silicon and may deflate over time, it is assumed that the vessel will remain permanently occluded because of the associated thrombus formation. Balloons are suitable for treating high flow pulmonary AVM's as well as a large vessel AVF's.

Mechanism of Action: cause mechanical obstruction are reserved for AVF and venous occlusions.

Sclerosing Agents

A. Ethanol

Ethanol preparations suitable for sclerotherapy include 95% or 98% dehydrated forms, generally available through hospital pharmacies for

neurolysis. Ethanol rapidly denatures proteins in the endothelial lining of vessels and, in stagnant channels, results in immediate thrombosis.

Having a low viscosity, it passes readily through arteriovenous shunts making it suitable for embolisation of AVM in conjunction with supra-selective catheterization of the nidus. It should never be injected into a proximal feeding artery, as penetration of the capillary bed will result in severe tissue necrosis.

Ethanol also causes neurolysis locally. Systemic effects include CNS depression, hypoglycemia, hypertension, hyperthermia, cardiac arrhythmias, pulmonary vasoconstriction and pulmonary hypertension, and electromechanical dissociation.

Cardiovascular collapse, sometimes fatal, can result from effects on the pulmonary vasculature or myocardium. To avoid this, ethanol should be administered in small aliquots, with adequate time for recovery between injections. Consideration should be given to monitoring of pulmonary artery pressure. A total dose of 1 ml/kg or 60 ml should not be exceeded in one procedure.

B. Detergent Sclerosants

This category includes sodium tetradecyl, the most commonly used sclerosant, ethanolamine and polydocanol. Like alcohol, these sclerosants damage the endothelial cells and cause coagulation of the intraluminal blood products. Detergent sclerosants can be opacified with water-soluble contrast medium or with oily contrast medium. Addition of air results in a microfoam which is felt to be more effective than the bland solution. A reasonable dose limit for image-guided sclerotherapy is 0.5 ml/kg or 30 ml.

C. Other Sclerosants

Doxycycline is available as a powder that can be suspended in saline or contrast medium and is often used for sclerotherapy of lymphatic malformations. It is painful to inject, but effective and relatively nontoxic. An advantage in treating large lymphatic malformations is that large volumes can be used in a single session.

Bleomycin has been used for decades in the sclerotherapy of lymphatic malformations (LM). It has some systemic side effects including pulmonary fibrosis, hair loss and pigmentation and therefore the quantity of this drug used in each session must be carefully limited.

Mechanism of Action: Intravascular use of sclerosants results in thrombosis, swelling and hemolysis. Large quantities of sclerosants result in hemoglobinuria requiring aggressive hydration and urine alkalinisation.

Embolisation of High-flow Vascular Malformations (AVF & AVM):

Preoperative embolisation aims to occlude selectively the arterial supply to the lesion, in order to reduce bleeding during operative resection. The embolic material should be chosen to occlude the most distal feeding arteries (Onyx or Glue), avoiding proximal occlusion especially with permanent devices (Coils or Balloons), and avoiding embolisation of normal tissue with excessively small particles (PVA).

PVA particles greater than 250 microns are relatively safe in terms of avoiding damage to adjacent skin or nerves.

Primary embolisation usually involves serial embolisation using ablative agents.

Intranidal injections of Ethanol may sometimes be helpful to achieve more permanent occlusion.

Sodium tetradecyl should not be used intra-arterially as it causes excessive arterial spasm and reflux.

AVM's

Direct arteriovenous communications are curable if the actual shunt or the immediate draining vein is occluded with a permanent device e.g. Detachable Balloons, Coils or NBCA.

AVF

In occluding large AVF, some type of flow control may be necessary to prevent migration of the Balloons or Coils. Upstream or downstream angiographic balloon catheters and tourniquets are often used.

Side-to-side fistulas can be occluded using covered stents.

Occlusion of Low-flow Vascular Malformations (VM)

VM

VM is the most common symptomatic vascular malformation referred for treatment. The basic defect in this lesion is maldevelopment of the vessel wall, especially the muscular media, resulting in abnormalities of shape and size of the affected vessels. There are a large variety of morphological types and venous malformations that can involve all tissue planes. VM can be sequestered, in which case sclerotherapy is safe and simple to perform, or non-sequestered, involving channels that communicate directly with major conducting veins. In the latter situation, precautions must be taken to isolate the treated segments of veins, to retain the sclerosant and subsequent thrombus. Failure to do so not only carries a risk of systemic complications and

pulmonary embolus, but usually results in prompt recanalization. Outflow occlusion can be achieved temporarily by the use of an occluding tourniquet (sterile orthopedic automatic tourniquet), or permanently by occluding the outflow veins with Coils, Balloons or NBCA.

Variceal masses protruding from conducting veins can be sclerosed effectively with the combination of intraluminal fibered coils and sclerosant.

Sclerotherapy of VM is usually performed with ethanol or sodium tetradecyl.

Endovenous ablation has been applied to venous malformations and appears to be safe and effective, but the longterm outcome is not yet known.

LM

Lymphatic Malformations (LM) are generally classified as macrocystic, microcystic and mixed forms.

Macrocystic forms respond best to resection or sclerotherapy. Intracystic fluid should be aspirated prior to the injection of the sclerosant. Aspiration of fluid and injection of sclerosant can then be monitored by continued ultrasound imaging. This technique is also helpful in injecting microcysts, where fluid aspiration and contrast injection generally are not feasible.

Complications:

Tissue necrosis

Damage to skin or more extensive tissues is the most common complication of liquid embolisation or sclerotherapy of vascular malformations. Approximately 5-10% of patients having sclerotherapy of venous malformations have some skin necrosis resulting in scarring. In many of these cases such scarring is inevitable since the malformation involves the skin. Ulcers are treated with topical antibiotic ointment or polymer dressings and most heal well.

Tissue damage caused by reflux of sclerosant into nourishing arteries can be extensive, resulting in loss of digits or limbs or requiring debridement and skin grafting. Sclerosing agents injected into the venous component of AVM can enter the arterial circulation when the venous outflow is completely occluded.

Nerve Injuries

Neurologic injury can result from three mechanisms. Extravasation of ethanol around a nerve trunk can result in a demyelination and necrosis. Penetration of arteries supplying nerve trunks can result in ischemic necrosis. Severe swelling caused by intravascular sclerotherapy can cause compartment syndrome and subsequent nerve injury.

Hematologic Effects

Endovascular treatment of large vascular malformation results in intravascular thrombosis and consumption of clotting factors. In patients with extensive venous malformations, this may be significant. Patients with preexisting consumption coagulopathy can be pretreated with Heparin to build up their fibrinogen stores, thus minimizing this complication. Such patients also often require infusion of plasma or cryoprecipitate.

Pulmonary Embolism

Massive pulmonary embolism is a rare complication of embolisation of malformations involving large conducting channels. Migration of microthrombi during sclerotherapy can also affect the pulmonary vascular reserve and result in cardiovascular collapse. In neonates, right-to-left shunting across a patent foramen ovale can cause systemic embolisation sometimes resulting in stroke or death due to myocardial infarction.

Hemoglobinuria

This complication is frequent and generally not significant if the patient is well hydrated and the urine is alkalinised. However in the presence of poor hydration, it can result in acute renal failure requiring hemodialysis.

Consumption Coagulopathy

Consumption of fibrinogen during sclerotherapy can be significant.

Systemic Effects of Ethanol

The most common systemic effect of ethanol is CNS depression. This can be significant in patients having general anesthesia or receiving narcotic analgesia. Cardiovascular affects include cardiac arrhythmias during and after the procedure, severe hypertension following the procedure, and introprocedural pulmonary vasospasm and cardiovascular collapse.

Acute desaturation with bradycardia can also occur during ethanol sclerotherapy. Usually, this is reversible with cessation of injection, administration of atropine and 100% oxygen.

Other systemic adverse affects include hyperthermia, severe hypertension and hyperglycemia.

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A/Prof Lourens Bester
St Vincent's Hospital,
Sydney.