The Art and Science of Infusion Nursing

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Accidental Intravenous Infusion of Air

A Concise Review

ABSTRACT

The unintended intravenous infusion of small volumes of air is common in clinical practice. International Electrotechnical Commission guidelines for infusion pumps permit infusion of up to 1 mL in 15 minutes and discount bubbles smaller than 50 µL. A review of the literature, however, suggests that these limits may be too generous. Neonates and patients with right-to-left cardiac shunts (eg, patent foramen ovale [PFO]) are at risk from lower volumes. Because PFO is prevalent in 20% to 27% of healthy adults and generally asymptomatic, all patients are at risk from small air bubbles, although clinically significant air embolism from intravenous infusion is rare. Attention to good clinical practice and use of an inline air filter should be considered to reduce any risk.

Key words: air embolism, adverse events, infusion, intravenous

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Dr Wilkins received payment from B. Braun Medical Inc. for writing this article and serves as a paid consultant to the company. Dr Unverdorben served B. Braun of America, Inc. as the chief medical officer and senior vice president of medical scientific affairs. The authors of this article have no further conflicts of interest to disclose.

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DOI: 10.1097/NAN.0b013e31827079fe

When a drug bolus is injected from a syringe, good clinical practice is to both eject all air from the syringe and to aspirate blood into the syringe before injection. However, use of infusion systems (gravity bags or pump driven), despite adequate priming, may cause small air bubbles to develop and then increase in size because of the effects of temperature and pressure changes (Edwin Burnard, ME, MBA, oral communication, August 2011). If not used in accordance with the instructions, connection devices may be associated with a small amount of air that may not be detected before injecting the fluid. The risk of air injection can be reduced by careful handling of intravenous administration devices; air sensors in intravenous infusion pumps can detect air upstream of the sensor, and air elimination filters can prevent air injection, although their use adds to the cost and complexity of the infusion system.

Electromechanical systems are widely used for the administration of fluids and parenteral drugs. Despite the best efforts of health care professionals responsible for managing intravenous drug delivery, from time to time visible and invisible air bubbles may accidentally be infused into the patient. The International Electrotechnical Commission (IEC) has developed a standard that addresses this issue.[1] The IEC standard states: "Infusion of 1 mL (12.4 mm diameter [calculated as if the bubble were a sphere]) of air within 15 minutes is not considered to be a safety issue. Bubbles of less than 50 µL (4.6 mm diameter) of air each are omitted in summing up the 1 mL."[1(p50)]

These guidelines may not, however, be very useful clinically. Visible bubbles may raise concern for the staff and the patient, and patients of different ages/sizes and with different preexisting conditions may vary in their susceptibility to harm from air injection or infusion, making a single recommendation inappropriate. Therefore, this paper reviews current knowledge and guidelines regarding air bubbles in intravenous lines and discusses possible solutions to the problem.

METHODS

The authors identified appropriate publications for review using PubMed[2] literature searches conducted during November 2011, the first using the terms *air* and *intravenous* and the second using *air* and *embolism* and *reviews or meta-analyses*. The second search was intended to ensure that the health consequences of air from any source were adequately identified. The searches identified 1752 citations, and the authors selected 83 for detailed review on the basis of the apparent relevance of the abstract, or title if no abstract was available.

The literature identified can be categorized into 4 groups:

1. animal studies describing the pathophysiology of air injection
2. theoretical and animal studies describing the behavior of injected air
3. reports of accidental air administration to patients in unusual circumstances or following a medical mishap
4. reports of air infusion during routine care of a peripheral or central intravenous catheter.

This review focuses primarily on the last group of publications; the other publications provide supportive data.

RESULTS

Physics of Air Bubbles

Air in static fluids typically takes the shape of a bubble to reduce surface tension. Several smaller bubbles form bigger bubbles. Air in fluid that is in small tubes loses the bubble shape when touching the tube. In laminar currents, air bubbles tend to travel in the center of the stream and tend to accept a more elliptical shape. Air bubbles occur in tubes such as infusion systems mainly by injection from the outside but may enlarge during passage (Edwin Burnard, ME, MBA, oral communication, August 2011). The number, shape, and size of air bubbles determine how they travel within the infusion system and their effects in the human body.

Incidence of Air Bubbles

Use of intravenous infusion pumps and sets, despite adequate priming, may be associated with the infusion of small air bubbles. Small air emboli, detectable by electron beam computed tomography (CT), were found in 4.8% of patients after insertion of a peripheral venous cannula.[3] Air was identified in the pulmonary trunk in 6 of 10 patients, in the right ventricle in 2 patients, in the right atrium in 1 patient, and in the left brachiocephalic vein in 1 patient; all patients were asymptomatic. Venous air bubbles have been identified in 15% of patients undergoing contrast-enhanced CT of the head and neck.[4] However, the authors could find no studies that describe the incidence rate of intravenous air infusions identified by consequent clinical symptoms and signs, and case reports are rare. This is in contrast to the situation when larger volumes of air enter the venous circulation after the accidental opening of a central venous catheter to the atmosphere; fatality rates of 32% have been identified in a series of case reports of air embolism associated with central venous cannulation.[5]

Pathophysiology of Air Bubbles

Comprehensive descriptions of the underlying physics of air bubble behavior and of the pathophysiology of air embolism are available.[6] Air bubbles damage tissues in 2 ways:

- an immediate obstructive ischemic effect, when the bubble occludes a blood vessel
- by provoking a longer-term thromboinflammatory response at the tissue-microbubble interface

The lungs act as a filter; bubbles >20-30 μm in diameter (4.2-pL volume) cannot pass through. Bubbles in vivo adopt shapes ranging from the almost spherical to the almost cylindrical, and absorption time varies with both volume and shape. Spherical bubbles of a given volume have the greatest diameter (and, thus, may occlude a larger vessel) but have the faster absorption time; cylindrical bubbles have a larger surface area, thus provoking a greater inflammatory response, and are most slowly absorbed. A 10-nL (2.7-mm diameter) bubble may take 20 to 30 minutes to absorb, and a 2.5-nL (1.7-mm diameter) bubble may take 9 to 13 minutes, depending on the bubble geometry.[7] Bubbles have a prolonged life in the human circulatory system when compared with the life span of a sphere-shaped bubble in water.[8]

Clinical Consequences of Air Bubbles

The clinical consequences of intravenous air depend on the volume and rate of injection. Acutely lethal volumes are 0.5 to 0.7 mL/kg in rabbits and 7.5 to 15 mL/kg in dogs; in human adults, the acutely lethal volume is about 3 to 5 mL/kg,[9] although a case report[10] describes survival of an infant after peripheral administration of 12 mL of air (3.5 mL/kg). Fatal air embolism has occurred with flow rates of 1 mL/kg/s[11]; injection of 50 mL of air at 1 mL/s (~0.02 mL/kg/s) into an adult male undergoing CT examination has been reported without significant adverse effects.[12] Standard intravenous delivery techniques are capable of delivering a fatal air infusion: a pressure decrease of 5 cm H_2O across a 14-gauge needle (internal diameter of 1.8 mm) is capable of transmitting approximately 100 mL of air per second.[13]

If the infused air remains in the venous circulation, symptoms range from none to cardiopulmonary collapse from right ventricular outflow obstruction. In symptomatic air embolism, hypoxemia and hypotension are usual; inflammatory changes produced in the lung lead to increased airway resistance.[14]

Paradoxical Air Embolism

Paradoxical air embolism occurs when the air enters the circulation on the venous side but creates effects in the systemic/arterial circulation. Air may pass through the pulmonary vasculature, or through cardiac defects, of which the most common is a patent foramen ovale (PFO). The prevalence of PFO in the general population is 20% to 27%, with a higher prevalence in younger patients and a lower prevalence in the elderly.[15,16] PFO is generally asymptomatic. Although there may not be a persistent right-to-left flow of blood, a bubble of air may pass from right to left during transient periods of elevated right atrial pressure—during coughing, for example.[17] The presence of a PFO is associated with arterial embolization of air following intravenous air. In a review of 26 cases of cerebral air embolism associated with intravenous air as a complication of central venous cannulation, a PFO was reported in 40%.[18] In neonates, the foramen ovale is often patent for the first several days of life. Interatrial flow persists in 19% of neonates at 4 to 5 days of age[19] and may be present for an extended period after birth.[20] A PFO or other anatomic shunt is not required, however, for gas to pass from the venous to arterial circulation: the lungs have an effective filtration threshold of about 0.35 mL/kg/min, after which arterial bubbles are detected in 50% of subjects.[21]

End-Organ Damage

Infused air, if it reaches a vulnerable end organ such as the heart or brain, may produce tissue necrosis. An intracoronary air dose of 0.02 mL/kg was associated with 28% mortality in a canine model.[22] During a case of intracoronary air embolism while a patient was undergoing a stenting procedure, small air bubbles were detected on fluoroscopy, and the patient developed chest pain and hypotension.[23] Bubbles less than 15 µm in diameter (volume < 2 pL) pass freely through the cerebral circulation, whereas bubbles with diameters greater than 200 µm (volume > 4 nL) become trapped in cerebral arterioles for variable periods and are associated with ischemia during in vivo studies.[24]

DISCUSSION

Some of the data reviewed here were published before the year 2000. Because the papers describe the basic pathophysiology of intravenous air infusion, the work has not been repeated in recent years, and it is helpful to this discussion. As the volume of air infused increases, adverse clinical events become more common; the available data are summarized in Table 1.

TABLE 1

Summary of Observed and Predicted Effects of Increasing Air Volumes

Bubble Diameter	Bubble Volume[a]	Bubble Length in Standard IV Tubing[b]	Equivalent Volume in a 70-kg Adult	Equivalent Volume in a 3-kg Neonate	Event/Notes
0.2 mm[25]	0.004 µL	1 µm			Detectable cerebral ischemia
0.3 mm[6]	0.010 µL	1 µm			Takes up to 30 min to absorb
3.4 mm[5]	20 µL	2.8 mm			Can pass through lungs
4.6 mm (E. Burnard, personal communication, 2011)	50 µL	7.1 mm			Discounted by IEC standard
4.8 mm (neonate), 14 mm (adult)[23]	0.02 mL/kg	8.5 mm (0.06 mL), 19.8 cm (1.4 mL)	1.4 mL	0.06 mL	28% mortality if entering the coronary circulation
12.4 mm (E. Burnard, personal communication, 2011)	1 mL	14.1 cm			Accepted as safe within a 15-min period by IEC
1.8-2.1 cm[9]	3-5 mL/kg	>1 m	210-350 mL	9-15 mL	Acute adult lethal volume

[a] *Computed as if a sphere:* $V = \frac{4}{3}\pi r^3$.

[b] *Three-millimeter internal diameter assumed; bubble length calculated as if a cylinder.*

Abbreviations: IEC, International Electrotechnical Commission; IV, intravenous.

Although the passage into a patient of a few bubbles of air is a common occurrence, there is no substantial body of literature describing consequent adverse events. In intravenous tubing of internal diameter 3 to 4 mm, these bubbles will have a volume of ~15 μL and are small enough to pass through the lungs to the arterial circulation, and yet they are large enough to cause cerebral ischemia. Bubbles of this size will take more than 30 minutes to be absorbed, and it must be assumed that on the vast majority of occasions they lodge in tissues without creating a detectable pulmonary or arterial embolic event. Given the common occurrence of asymptomatic PFO, it should also be assumed that bubbles of any size have the potential to cross into the arterial circulation and create cerebral or coronary ischemic events.

Neonates are a high-risk population because PFO is more common in neonates and their body mass is lower. At the lower limit of viability of about 600 g,[25] an equivalent to a fatal dose in adults of 3 mL/kg may be only 2 mL; the case of a 384-g neonate who developed fatal peripheral air embolism with repeated injections of 0.02 mL of air during intravenous drug administration[26] has been recorded.

Pathophysiologic effects have been described even after exposure to very small (<1 μL) bubbles, supporting the contention that there is no safe maximum dose of intravenous air, and all reasonable steps should be taken to minimize any intravenous air injection. Air-in-line sensors in intravenous infusion systems should be used when available. Although there are no controlled clinical studies demonstrating their benefits in avoiding air embolism, a 0.2-μm in-line filter will prevent infusion of air.

Treatment of air embolism depends on the site of ingress, volume of air, and patient condition. In general, ensure that no further air is injected, consider attempting to aspirate air from the right heart, and institute cardiopulmonary support if required.[9]

CONCLUSIONS

In conclusion, the IEC standard does not represent a universally safe level of air infusion; indeed, from the data reviewed, there is no demonstrable maximum safe dose of air infusion. Bubbles as small as 0.004 μL may create cerebral ischemia; such bubbles are significantly smaller than the 50-μL bubbles that are disregarded by the IEC. One milliliter of air infused over 15 minutes, the upper limit in the IEC standard, is close to the 1.4-mL dose that would be potentially fatal in the coronary circulation of an adult, and well above the volume associated with potential fatality in neonates. Moreover, the IEC standard does not explain how often volumes below 1 mL may be safely infused over subsequent periods of 15 minutes.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Although clinical consequences of air infusion are rare, patient risk can be minimized in 2 ways: by appropriate design of infusion systems and by adherence to the highest standards of clinical practice. Adult infusion systems should be designed to prevent infusion of volumes of air >50 μL in normal use and to prevent infusion of volumes of air >1 mL in failure modes. For neonatal and infant use, systems should be designed to minimize the volume of air infused to the lowest level possible, compatible with device function. Air infusion volumes of 10 μL should not be exceeded even in failure mode. Although the IEC standards apply to intravenous pumps, similar considerations apply to gravity infusion systems. Good clinical practice includes aspiration of air from stopcocks and needle-free connectors before injection and expelling all air from syringes. Most important, even small volumes of air should be considered as potentially consequential. Although there are no data available from adequately designed clinical studies, the safest available approach is the use of an air elimination filter. Available from several manufacturers, air elimination filters can function in any orientation and also remove bacteria and particulates from the infusion.

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