REVIEW

Intravenous therapy

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Intravenous administration of fluids, drugs, and nutrition is very common in hospitals. Although insertion of peripheral and central cannulae and subsequent intravenous therapy are usually well tolerated, complications that prolong hospitalisation, and in some cases cause death, can arise on occasions. Additionally, many cannulae are inserted unnecessarily. This article seeks to review this area and to outline good medical practice.

In modern medical practice, up to 80% of hospitalised patients receive intravenous therapy at some point during their admission.[1 2] Medication, fluids, nutrition, and blood products can all be given via the intravenous route, which can be either peripheral or central. Although common, these practices are not devoid of complications, which may lead to mortality and morbidity, increased duration of hospital stay, and significant costs.

PERIPHERAL VENOUS CANNULATION

Peripheral venous cannulation is the commonest method used for intravenous therapy. There are numerous well recognised indications (box 1) and contraindications (box 2) for peripheral venous cannulation, but, despite these, there is no doubt that many intravenous lines are inserted unnecessarily.[4] In a study of almost 1000 patients in general medical beds, ''idle'' intravenous cannulae (a cannula not used for 48 hours or with no prophylactic indication) were identified in 33% of patients.[5] In order to improve clinical practice, hospital guidelines were developed, largely by junior medical staff.[6] A follow up study after implementation of the guidelines showed that the rates of ''unnecessary cannulation'' had fallen significantly. A French study also found that 28% of peripheral cannulae inserted in an emergency department were ''unjustified'',[7] and a smaller audit in our acute medical unit found the rate of apparently unused cannulae to be almost 50% (C Waitt, unpublished data).

Therefore, before a cannula is inserted it is important to ask whether it is clinically necessary. In some cases, a cannula is never used but its insertion is medically justifiable on a prophylactic basis in patients with serious and/or unstable disease, where intravenous access may be needed in an emergency. In most cases peripheral venous cannulae are used for administration of fluids; before a decision is made to do this, it is essential to question whether the administration of intravenous fluids is both appropriate and necessary.

Is administration of intravenous fluid appropriate?

Fluid and electrolyte disorders and acid-base imbalance are very common in hospital inpatients, but they are often mismanaged. A report by the National Confidential Enquiry into Perioperative Deaths criticised the fluid management of elderly patients.[8] This may reflect inadequate training of junior hospital doctors, who are responsible for most of the prescriptions for intravenous fluids. For instance, an evaluation of the level of training and the clinical practice of pre-registration house officers and senior house officers in South Wales showed that 58% had never received any formal teaching on the subject and that 36% did not check either the clinical details or the blood results before prescribing intravenous fluids.[9] Detailed discussion of fluid, electrolyte, and acid-base balance is beyond the scope of this review, but valuable information can be obtained from standard physiology and anaesthetic textbooks. It should be emphasised that prescription of fluids deserves the same status as prescription of drugs.

Is administration of intravenous fluid necessary?

Dehydration is an important clinical problem for which intravenous fluids are often prescribed. However, even in such circumstances, it may not always be necessary to use intravenous fluids. For example, in children, there is a wealth of evidence supporting the use of oral rehydration therapy in dehydration, particularly that caused by acute gastroenteritis.[10–12] This can be effective even in patients with vomiting, and can be administered via the nasogastric route in the event of the patient being reluctant to drink.[13] In comparison with the intravenous route, proven benefits include financial savings,[14] improved clinical outcomes, decreased workload for medical and nursing personnel, decreased rates of hospital admission, and avoidance of intravenous cannulae and their associated complications.[11] No studies have been undertaken in adults into the use of oral rehydration therapy.

Elderly and terminally ill patients are also prone to dehydration and electrolyte derangement, and, as in children, intravenous cannulation is often difficult and poorly tolerated. Hypodermoclysis, or subcutaneous administration of fluid, was widely used at the start of the 20th century.[15 16] The technique fell out of favour in the 1950s after reports of severe adverse reactions to the misuse of electrolyte-free or

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Abbreviations: CR-BSI, catheter related bloodstream infection; GTN, glyceryl trinitrate

Box 1: Indications for peripheral venous cannulation

- Intravenous fluids.
- Limited parenteral nutrition.
- Blood and blood products.
- Drug administration (continuous or intermittent).
- Prophylactic use before procedures.
- Prophylactic use in unstable patients.

Adapted from Datta *et al*.[3]

Box 2: Contraindications and cautions for peripheral venous cannulation

- Inflammation or infection of the insertion site.
- Forearm veins in patients with renal failure (may be needed for arteriovenous fistulae).
- Irritant drugs into small veins with low flow rates (that is, leg and foot veins).

hypertonic solutions.[17] Over the last 20 years, hypodermoclysis has increasingly been rediscovered as an ideal technique for administering fluid in certain populations.[18] A recent randomised comparison of intravenous and subcutaneous fluids in an elderly population demonstrated improved patient satisfaction, lower rates of cellulitis and thrombophlebitis and equivalent efficacy in terms of rehydration and correction of electrolyte abnormalities.[19] There may also be significant financial benefits.[20] In patients receiving palliative care, hypodermoclysis has the added advantages that it is easy and safe to administer at home, and insertion of the catheters requires little training and thus can be performed by family members.[21] Hypodermoclysis has largely been restricted to the above patient groups, and, given the many benefits of this technique, further evaluation is certainly indicated, particularly in settings where resources are limited.

ADMINISTRATION OF DRUGS BY THE INTRAVENOUS ROUTE

Drugs are also frequently administered by the intravenous route, either as bolus injections or by infusion. The indications for the intravenous administration of drugs can be summarised as follows:

- If the patient has a serious disease, the administration of a drug intravenously may have advantages over oral drug administration in terms of reducing mortality. This is perceived to be the case in patients with life threatening bacterial infections. Although the use of intravenous antibiotics may often be indicated in patients with serious infections, it is common practice in hospitals to start intravenous antibiotics irrespective of the severity of the infection. Oral antibiotics in most of the patients admitted to hospital with bacterial infections are just as effective as intravenous antibiotics and have the added advantages of ease of administration, reduced labour and administration costs, and reduced hospital stay.[22 23]
- The drug may have limited oral bioavailability or only be available in an intravenous preparation; for example, aminoglycoside antibiotics are polycations and highly polar and thus will not be absorbed via the gastrointestinal tract; therefore, they have to be administered parenterally.
- The patient may be unable to take medications orally because of vomiting or may be ''nil by mouth''. In these circumstances, other routes such as rectal, sublingual, subcutaneous, and intramuscular should be considered.
- The patient may have an impaired conscious level and be at risk of aspiration; again, alternative routes should always be considered.
- Rapid peak drug levels may be required; these can be achieved by a bolus intravenous injection, which leads to a rapid and predictable increase in the blood concentration of the drug. This argument is often put forward for the use of antibiotics, but it is important to remember that many antibiotics have good oral bioavailability and will achieve adequate blood concentrations to inhibit bacterial growth.

GOOD CLINICAL PRACTICE IN PERIPHERAL VENOUS CANNULATION

Once a decision has been made to insert a cannula into a peripheral vein, it is important to obtain informed verbal consent from the patient (where possible) and to explain both the procedure and the need for cannulation. Although the risk of infection with cannulation is low,[24] it is important to maintain good aseptic technique to minimise the risk of local and systemic infections.

Choice of cannula

The flow rate through a cannula is proportional to the height of the fluid reservoir and the fourth power of the cannula's radius. Thus, doubling the cannula's diameter increases the flow by 2^4 (16-fold). For infusions of viscous fluids such as blood, and for rapid infusions, the largest cannulae (14–16 gauge) should be used. Smaller sizes (18–20 gauge) should suffice for crystalloids. The smallest cannulae (20–24 gauge) are adequate for the intermittent administration of drugs, except those that must be given by rapid infusion.

Selection of a vein

Veins on the non-dominant forearm are most suitable, especially if the cannula has to remain in position for any length of time. Veins on the dorsum of the hand are easiest to cannulate, but are more uncomfortable for the patient and more liable to block. Veins in the lower limb should be avoided where possible because of the increased incidence of thrombophlebitis and thrombosis.[25]

Obtaining venous access in difficult situations

Various strategies can be employed if it is difficult to identify a vein that is suitable for cannulation. A tourniquet should be applied 5–10 cm proximal to the selected site. The compression must permit arterial inflow while restricting venous outflow. In order to do this more accurately, a sphygmomanometer cuff inflated to diastolic pressure can also be utilised.[26] Warming of the limb improves peripheral vasodilatation. This can be done with warmed poultices or a basin of water. Using a carbon fibre ''warming mitt'', which was designed to provide reproducible amounts of heat, Lenhardt *et al* concluded that local warming facilitates the insertion of peripheral venous cannulae, reducing both the time and number of attempts required.[27] Topical venodilatation may also be achieved by applying 4% nitroglycerine ointment, smeared onto the skin and left for 2–3 minutes.[28 29]

Ultrasound guided venepuncture is an established technique for both peripherally inserted central catheters and central venous cannulation.[30] It has been suggested that, with the increasing availability of portable ultrasound facilities, this may become an option in the future for difficult peripheral venous cannulations.[31] Indeed, a hand held Doppler probe has been used to identify accurately forearm

veins of more than 2 mm diameter in patients with invisible and impalpable veins.[32]

In neonates, vascular access can be obtained via the umbilical vein, although this has been associated with portal vein thrombosis.[33] In infants, scalp veins are often amenable to cannulation, and central catheters can also be inserted by this route.[34] Intraosseous infusions have also been used for fluid administration in haemodynamically compromised children, although care must be taken with needle placement in order to avoid injury to epiphyseal growth plates.[35]

In emergency situations, particularly in hypotensive trauma victims, peripheral venous cut down is a viable option. A skin incision can be made directly over either the long saphenous vein in the ankle or the median basilic vein in the elbow. The vein is exposed by blunt dissection and cannulated under direct vision after making a small incision in the wall and ligating the distal end.[36] Intraosseous infusion may also be used in such patients,[37 38] even in bones that do not contain a medullary cavity.[39] In extreme situations, the corpus cavernosum can be cannulated for purposes of resuscitation.[40]

Finally, when peripheral venous access cannot be obtained and there is a need for intravenous therapy, placement of a central venous line should be considered. Although this is a last resort as a simple substitute for peripheral access, central venous access may be indicated for other reasons, as discussed below. In addition, the morbidity in critically ill patients is lower from centrally inserted central catheters than from peripheral intravenous catheters.[41]

Use of local anaesthetic

The majority of junior doctors do not use a local anaesthetic when performing peripheral venous cannulation. In a survey of 71 pre-registration house officers, local anaesthesia was not used because it was too time consuming (45%), because it was felt not to be indicated (35%), because it made cannulation more difficult (21%), because of lack of availability of the local anaesthetic (13%), because of logistical difficulties (13%), because of peer pressure not to use it (4%), and because of practical difficulties (3%).[42] In addition, it is felt by many that the pain caused by injection of local anaesthetic is equivalent to the pain of cannulation.[43] However, these views are not borne out in controlled studies. For example, Holdgate and Wong performed a randomised trial using preprepared cannulation packs, 50% of which contained local anaesthetic. They found that subcutaneous lignocaine did not adversely affect the success rate of intravenous cannulation on the first attempt and significantly reduced the pain associated with cannulation.[44] In a direct comparison, subcutaneous lignocaine was found to be superior to ''eutetic mixture of local anaesthetics'' (EMLA) topical cream, with the added advantage that cannulation can be attempted after 30 seconds rather than after an hour.[45] Other studies have borne out the benefits of topical or subcutaneous anaesthesia prior to cannulation.[46 47] In paediatric practice, it is now commonplace to use topical anaesthesia prior to either venepuncture or cannulation, but this is not the case in adult medicine. Although some authors have suggested that the use of local anaesthesia should become standard practice,[46 47] further studies examining the clinical and cost effectiveness of this strategy need to be performed before it can be recommended as routine practice.

Duration of peripheral cannula use

The most common complications of peripheral venous cannulation are thrombophlebitis and extravasation.[48–50] These result in an inflammatory reaction, which is manifested as pain, swelling, and erythema. In some patients, this can progress to local or systemic infection and, in rare cases, may result in a pulmonary embolism.[1] This inevitably leads to increased workload for medical and nursing staff, and, in some cases, prolongs the duration of hospital stay.[51]

The rate of phlebitis increases with the time that the cannula remains in place,[52] and, for this reason, it is currently recommended that intravenous cannulae are routinely changed after 48–72 hours.[53 54] However, more recent studies have shown no increase in cannula related complications, including thrombophlebitis, when the duration was prolonged to 96 hours.[55 56] This suggests that routine replacement is not necessary, but that each cannula should be inspected daily and removed should there be any clinical evidence of infection.

Use of transdermal glyceryl trinitrate

Glyceryl trinitrate (GTN), a vasodilator predominantly acting on the venous side, has been used to prevent infusion failure.[1] Two randomised controlled trials have shown that transdermal GTN reduced the rate of infusion failure by up to 70% compared with a placebo.[57 58] However, some of the patients on the GTN patches suffered headaches and local skin reactions, and the dosing strategies in the two trials were different. An economic analysis showed that the use of GTN patches may be cost effective only if the infusion time is likely to exceed 50 hours.[59] It seems that GTN is more likely to prevent infusion failures than are other preventive strategies (such as corticosteroids, heparin, and inline filtration), although there have been no comparative studies.[60] There is not enough evidence as yet to recommend the prophylactic use of daily GTN patches in all patients on intravenous infusions, but it is an option that should be considered in patients with poor venous access where intravenous therapy is likely to be required for longer than two days.

CENTRAL VENOUS CANNULATION

Central venous cannulation is increasingly used not only in intensive care and high dependency units but also on general medical and surgical wards. Indications for central venous cannulation are listed in box 3. Many problems can occur with the insertion of a central venous catheter, including arterial puncture, puncture of a lung leading to a pneumothorax, and perforation of the right atrium or pulmonary artery. Appropriate training and experience is essential in avoiding these complications, especially since the majority of central venous catheters are inserted by doctors in training. This has been recognised by the National Institute for Clinical Excellence in the UK, which has published guidelines that recommend two dimensional ultrasound guidance as the preferred method for cannulation of the internal jugular vein. The guidelines also stipulate that clinicians undertaking this procedure should receive appropriate training to achieve competence since the technique is operator dependent with a long learning curve.[61]

Catheter related sepsis

The most common complication observed with central venous catheters is local and systemic sepsis. Catheter related bloodstream infection (CR-BSI) is a serious nosocomial infection with substantial and directly attributable mortality and morbidity. It has been estimated that a single episode of catheter related bacteraemia costs $28 000 (£16 500) and has an attributable mortality of 10%–35%.[62] Various definitions have been used to describe sepsis related to catheters. The definitions proposed by the Centers for Disease Control[62] are among the most widely used, and are shown in box 4.

Epidemiology

The rates of CR-BSI vary between hospitals, clinical areas, and patient groups.[63] Overall, studies from Europe and the

Box 3: Indications for central venous cannulation

- Administration of irritant drugs, solutions, and nutrition.
- Monitoring of central venous pressure during fluid administration or resuscitation.
- Invasive monitoring of cardiac output.
- Insertion of temporary cardiac pacing wires.
- Obtaining venous access when this is not possible peripherally.

USA suggest that the usual incidence of CR-BSI, as a percentage of catheters inserted, is between 3% and 7%.[64]

Choice of site

The choice of site in an individual patient is a balance between the risks of mechanical complications, such as arterial puncture or pneumothorax, patient factors, such as aberrant anatomy or a previous difficult cannulation, and the risk of infection. In an emergency situation, the choice of site may differ from that used when a line is inserted electively. Several studies have demonstrated a significantly lower incidence of colonisation and CR-BSI in subclavian lines than in internal jugular lines.[65–67] This relates largely to the increased movement and exposure of the neck, the higher density of sweat glands, and the skin temperature.[68]

Skin asepsis

Most studies have shown high levels of concordance between micro-organisms found on the skin at the insertion site and organisms subsequently found on the catheter tip.[64] A study examining catheter tips immediately after insertion demonstrated a contamination rate of 16% caused simply by passing through the skin.[69] Therefore, aseptic technique is vital in preventing line infections, but unfortunately this is often neglected. A study from North Carolina investigated the impact of a one day course in infection control practices and procedures given to third year medical students and physicians completing their first postgraduate year. Attitudes towards sterile techniques were surveyed at baseline and after six months. In addition, rates of use of large drapes were recorded, as was the incidence of catheter related infection. After this simple educational intervention, there was a significant improvement in the understanding of aseptic technique accompanied by an increase in the use of large drapes and a corresponding significant decline in the rate of CR-BSI, together with financial savings.[70]

Along similar lines, a prospective cohort study of 3154 patients admitted to an intensive care unit was undertaken to evaluate the benefits of an educational programme.[71] This covered the following:

- Preparation of a ''trolley'' in advance.
- Skin preparation and disinfection (using alcohol based chlorhexidine gluconate 0.5%, with two minutes of drying time).
- Maximum barrier precautions (sterile gloves and gown, cap, mask, and large drapes) used for all but peripheral lines.
- The subclavian vein as the standard central insertion site.
- Dressings.

Once more, simple educational measures led to a statistically significant reduction in the rates of infection.[71]

Lack of adherence to asepsis continues to be a major problem. In our 1200 bed teaching hospital, an audit revealed that 50% of medical specialist registrars and 33% of medical senior house officers do not routinely wear a sterile gown while performing central venous cannulation. Lack of availability was a major reason for this (C Waitt, unpublished data).

Box 4: Centers for Disease Control definitions of sepsis related to central venous catheters

Colonised catheter
Growth of >15 colony forming units (semiquantitative culture) or >103 (quantitative culture) from a proximal or distal catheter segment in the absence of accompanying clinical symptoms.

Exit site infection
Erythema, tenderness, induration, or purulence within 2 cm of the skin at the exit site of the catheter.

Tunnel infection
Erythema, tenderness, and induration in the tissues overlying the catheter and >2 cm from the exit site.

Catheter related bloodstream infection (CR-BSI)
Isolation of the same organism (identical species and antibiogram) from a semiquantitative culture of a catheter segment and from the blood (preferably drawn from a peripheral vein) of a patient with accompanying symptoms of BSI and no other apparent source of infection. In the presence of laboratory confirmation, defervescence after removal of an implicated catheter from a patient with BSI may be considered indirect evidence of CR-BSI.

Taken from NICE.[61]

Duration of use and scheduled replacement

Many studies have demonstrated that the incidence of CR-BSI increases with the duration of catheter placement.[64 67 72 73] It is therefore necessary to review the need for central access continually in each patient and to remove the line as soon as it is appropriate.

''Scheduled'' catheter replacement is a common practice and in some respects seems ''logical''. However, a systematic review of routine catheter replacements at three and seven days found no advantage over replacement only when deemed clinically necessary.[74] Another study actually reported increased infection rates where scheduled replacement took place.[75] Infection occurring at the time of insertion may account for these results.[69]

Choice of catheter

To minimise infectious complications, catheters with the minimum necessary number of lumens should be used. The aim is to minimise manipulation of the external portion of the catheter and the number of openings into the vascular system.[62] In order to reduce the rate of infections, over the past decade, central venous catheters impregnated with antimicrobials have been developed.[76 77] There are two commercially available central venous catheters impregnated with antimicrobials, one of which uses chlorhexidine and silver sulfadiazine, while the other uses a combination of minocycline and rifampicin. They are more widely used in the USA than in the UK. Individual studies have shown a reduction in rates of CR-BSI with the use of these catheters,[78 79] and they have been hailed as a ''most significant advance'' in reducing rates of CR-BSI.[80] However, controversy still surrounds their use: a recent

analysis of 11 trials failed to demonstrate that antimicrobial impregnated central catheters were effective in preventing CR-BSI and suggested that there were many methodological flaws in the individual trials.[81] Antimicrobial-impregnated catheters have other limitations including a limited duration of antimicrobial activity, rare reports of anaphylaxis associated with use of the chlorhexidine catheter (interestingly occurring only in the Japanese), and concerns about the development of resistant organisms. Thus, further studies with more rigorous designs and clinically relevant end points are required before widespread use of central venous catheters impregnated with antimicrobials can be routinely recommended.

CONCLUSIONS

Peripheral and central venous cannulation are commonplace in the hospital environment but can lead to complications that cause patient morbidity and, in rare circumstances, mortality. It is therefore important to consider whether the patient needs a cannula inserted and, if there is genuine indication, to follow some of the simple measures outlined in this article to avoid complications. For central cannulae in particular, it is essential to ensure that insertion is performed using an aseptic technique. Once a cannula has been inserted, it is important not to forget about it, to review the need for it on a daily basis, and to remove it as soon as clinically indicated. Finally, there are many areas of current clinical practice where the evidence base concerning intravenous therapy is weak and needs to be strengthened by further research; these are listed in box 5.

Box 5: Areas requiring further research in relation to intravenous therapy

- Use of oral rehydration therapy in adults as an alternative to intravenous therapy.
- Use of hypodermoclysis in populations other than the elderly and the terminally ill.
- Clinical and cost effectiveness of routine local anaesthetic use in peripheral cannulation.
- Further evaluation of the routine use of GTN to prevent infusion failure.
- Rigorous studies of catheters impregnated with antimicrobials, with clinically relevant end points.

Learning points

- Many cannulae are inserted unnecessarily, so consider carefully the need for cannulation in every patient.
- There are many other routes for administration of fluids and drugs, which may be safer and more convenient than the intravenous route, and these should be considered in all cases.
- Local and systemic infections can complicate cannulation, and, particularly for central cannulation, aseptic technique is essential.
- Ultrasound guided venepuncture is an established technique for central venous cannulation and is in accordance with recent guidelines published by the National Institute for Clinical Excellence.
- Transdermal GTN prevents infusion failure and should be considered in patients with poor venous access if intravenous therapy is likely to exceed two days.
- Central catheters impregnated with antimicrobials may reduce the incidence of catheter related sepsis, but there needs to be further evaluation of their clinical and cost effectiveness.
- The need for peripheral or central cannulae should be reviewed on a daily basis and the cannula replaced or removed as clinically indicated.

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