Peripheral Intravenous Nutrition Therapy: Outpatient, Office-Based Administration

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Abstract
BACKGROUND: The use of peripheral intravenous nutrition (PIN) has been growing in recent years due to the increase in awareness of the pathophysiological mechanisms of peripheral vein thrombophlebitis, as well as the availability of techniques to prevent or retard its onset. With the increase in public and medical practitioner awareness of the importance of nutritional interventions in health and disease, more outpatient-based PIN therapy is being performed. Outpatient, office-based PIN has unique features including high osmolality, high infusion rates, and short infusion duration. METHODS: Previous intravenous nutrition studies were used to estimate safety parameters for outpatient, office-based PIN. CONCLUSIONS: Osmolalities of the infusion can approach 1000 mOsm/L if the duration of the infusion is only several hours. The infusion should be diluted to reduce the osmolality, even if an increase in infusion rate is necessary. Duration of infusion should be less than three hours to reduce the time the irritating mixture contacts the vein wall. This requires high (150 – 330 mL/hour) infusion rates. The largest vein, and smallest and shortest catheter possible to achieve the infusion rate desired should be used, with in-line filtration of at least 0.45mm. The cannula should be removed at the first sign of pain or redness. Standard procedures to reduce infection risks should be followed.
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Introduction

It has been estimated that 40 percent of all drugs administered in hospital settings is through injection.[1] Although indications for total parenteral nutrition (TPN) are diminishing as basic science and clinical studies continue to find increased benefits associated with enteral feeding, and as techniques for initiating enteral nutrition improve,[2] it remains in wide use, with 10 percent of ICU days using TPN.[3] The field of drug pharmacology and hospital-based intravenous administration is well researched, with tens of thousands of articles in the medical literature. Safety parameters including insertion site,[4-10] infusion rate,[11-20] osmolality of solution,[21-29] and time in situ[6,30-33] are well explored for hospital-based pharmaceutical and TPN infusions. However, safety parameters for outpatient, office-based peripheral intravenous (IV) nutrition infusions have not been explored in the literature to date.

With a substantial and rapid increase in the use of alternative medicine over the last decade, the focus of alternative medicine on proper nutrition, and the wide availability of pharmacological nutrient preparations for intravenous infusion, it is logical to assume the number of

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outpatient, office-based peripheral intravenous nutrition (PIN) infusions is increasing. Therefore, it is expedient to define safety parameters for office-based nutritional infusion therapy.

Most hospital infusions are delivered over a 12-24 hour time span because of patient around-the-clock availability, thus allowing a slower infusion rate but requiring longer retention of the catheter. In outpatient-based therapy, infusion rates are necessarily accelerated; therefore, the rate the infused solution comes into contact with the venous wall is increased. These differences may reduce some of the concerns regarding PIN, while increasing others. Risks of infection and septicemia have been correlated with infusion duration[5] and may be reduced in an in-office setting due to the decreased indwelling time of the catheter. Reductions in the risk of extravasation, catheter dislodgment, and occlusion would also be expected, due to the decreased time in situ. Additionally, there is a reduced need for patient movement while the line is inserted due to the short treatment time.

Complications of PIN include infection, phlebitis and thrombophlebitis, venous spasm, venous irritation, emboli, pain, hematoma or hemorrhage, extravasation, arterial cannulation, and needlestick injury.[34,35] Certain complications, such as venous irritation, venous spasm, and thrombophlebitis may exhibit an increased risk compared to hospital-based infusion due to the more rapid infusion rate. A slower infusion rate allows the admixture to dilute in a larger volume of blood, while a faster rate decreases dilution, allowing a possible osmotic or irritating component to more fully contact the venous wall.

One of the most common risks of intravenous therapy is phlebitis,[36,37] affecting almost 100 percent of patients in some studies.[22,38,39] Phlebitis causes severe discomfort in the affected limb, causing the vein to become red, swollen, and hardened.[35] Interruption of the therapy becomes necessary and a new site must be started.[40] Proper techniques of IV administration are well covered in many basic texts, and therefore will not be covered in this paper.

Thrombophlebitis is a thrombus within a vein with accompanying inflammation. The thrombus is initially composed of platelets and fibrin which then becomes interspersed with red blood cells. The inflammatory response in the vein is characterized by granulocyte infiltration, loss of endothelium, and edema. The symptoms of acute thrombophlebitis arise over a period ranging from hours to one or two days. The disease process is usually self-limited and lasts between one and two weeks, then the acute process subsides and painful symptoms disappear. Chemical phlebitis results from intimal injury induced by the introduction of catheters or noxious agents directly into a vein.[43]

Primary Considerations in PIN

Osmolality

Normal serum osmolality is 275-300 milliosmoles per liter (mOsm/L) depending on the source.[43,44] Excessive infusion of hypertonic fluids can lead to a variety of complications, including tissue irritation, pain, electrolyte shifts in the serum, red blood cell crenation, and general cellular dehydration. If the injection of a hypertonic solution is too rapid, blood pressure can fall, cardiac irregularities or arrest may occur, respiration can become shallow and irregular, and heart failure and pulmonary edema may result. This may be due to a large bolus of concentrated solute reaching the myocardium. Rapid infusion of hypertonic saline has also been shown to cause a sudden rise in cerebrospinal fluid.[45]

In PIN, the main effect of hyperosmolal solutions cited is phlebitis. Many studies have examined the effects of osmolality on the induction of phlebitis. Gazitua et al[22] found phlebitis was universal when osmolality exceeded 600 mOsm/L. They also found

phlebitis occurred more commonly with the use of solutions that contained amino acids. The important factors in the production of phlebitis by amino acid solutions were osmolality and the amount of potassium infused per day.

Bodoky et al[23] showed that an infusion solution including amino acids and carbohydrates with an osmolality of 1,100 m0sm/L exhibited no difference in peripheral venous thrombosis (PVT) after 48 hours compared to nutrition solution commonly used in hospitals such as Lactated Ringer's, five-percent glucose, and an electrolyte solution with osmolalities of 280-407 m0sm/L. Comberg et al[46] concluded that under normal clinical circumstances a hyperosmolar basic nutrition solution (806 mOsm/L) does not cause a higher rate of peripheral venous irritation compared with an iso-osmolar electrolyte solution, and should be administered to patients with an expected infusion time of not longer than four days.

Daly et al[47] studied 80 patients in four groups receiving infusions with osmolalities ranging from 630 to 983 mOsm/l. There was no difference in rates of phlebitis between patients who received peripheral infusion with high osmolar solutions compared to lower osmolar solutions.

Wilson et al[48] randomly allocated to two groups 20 patients who had undergone uncomplicated surgery of moderate severity who were fed using a peripheral vein for up to six days. Group I received a daily nutrient solution with an osmolality of 490 mOsm/kg, while group II received a daily solution with an osmolality of 376 mOsm/kg. Venous thrombophlebitis at the infusion site was assessed daily using Maddox's criteria,[49] with a minimal degree of inflammation which reached a maximum of 30 percent after five days.

Mattioli et al[50] used three standard lipid emulsion diets with final osmolalities not higher than 900 milliosmoles in 118 patients. Frequency and type of phlebitis were evaluated in patients submitted to PIN and in two groups of 10 patients who received five-percent dextrose in water (S-D5W) infusions and Protein Sparing Nutrition (493 mOsm/L) in the postoperative period. Frequency of phlebitis was significantly lower in PIN patients than in control patients. A treatment period of 15 days did not increase the frequency of phlebitis.

Kane et al[51] randomized 36 patients to either "high" (1700 mOsm/L) or "standard" (1200 mOsm/L) osmolality PIN feeding, with heparin added. Patients who received the 1200 mOsm/L feedings showed a mean duration of line survival of 6.8 days with eight cases of thrombophlebitis. This compared to a mean duration of line survival of 6.3 days with only four cases of thrombophlebitis in the 1900 mOsm/L group. The difference between groups was not statistically significant in either line duration or number of cases of thrombophlebitis. Increasing osmolality therefore, did not affect the rate of thrombophlebitis or the duration of line survival.

In a rabbit study, Kuwahara et al[18] examined the effect of dilution in reducing infusion phlebitis. Two solutions (784 and 718 mOsm/kg) were each infused at full strength and under dilution. The diluted solutions were infused at a faster rate, so that the actual amount of osmotically active particles per minute was similar between solutions. Phlebitic changes were observed in six of eight rabbits given solution A but in only one of eight rabbits given diluted solution A, although the same quantities of the same nutrients were infused. Changes were observed in six of eight rabbits given solution B, but in no animals given diluted solution B. These results suggest that osmolality of the infusion solution is an important factor in the development of phlebitis regardless of infusion volume or infusion rate, and that dilution is effective in reducing the phlebitic potential of infusion solutions.

Time In Situ

Weiss and Nissan[52] demonstrated a markedly reduced incidence of thrombophlebitis in patients who received intermittent intravenous infusions administered for a maximum daily period of 12 hours compared to continuous intravenous infusion therapy for more than 24 hours (4.4% and 20.3%, respectively).

Hessov et al[53] found that rates of thrombophlebitis in hospitals could be reduced by almost 40 percent (from 43% to 6%) by restricting infusion duration in the same vein to less than 24 hours, neutralizing sugar solutions with a phosphate buffer using the thinnest possible cannulas, administering vein irritant solutions as quickly as permissible, and using veins with the largest possible diameter. Additionally, no patient had more than one episode of infusion thrombophlebitis using these methods. A total of 196 patients received infusions over a total of 529 days in the study.

Lundgren et al[54] studied the relationship between time in situ and the frequency of thrombophlebitis. The frequency of thrombophlebitis was significantly higher and resulted in more troublesome and prolonged complications in the group receiving current hospital routines of time in situ of up to five days than in the experimental group with a time in situ of less than 24 hours.

May et al[31] examined several different PIN protocols and found severe phlebitis and line occlusion occurred more frequently in patients fed continuously over 24 hours compared to those fed over 12-hour periods. They concluded that infusion phlebitis may be minimized by reducing the time the vein wall is exposed to nutrient infusion.

A study using Serial B mode ultrasonographic imaging examined intraluminal thrombosis formation related to intravenous nutrition delivered via fine-bore catheters inserted into peripheral veins. Thrombus formation was detected in 14 of 22 catheterized veins; however, only nine episodes of clinical phlebitis occurred. Early thrombus formation, less than 24 hours, tended to be found close to the site of venipuncture, probably secondary to insertion trauma. Late thrombus formation was found at the catheter tip, where the hypertonic feed was delivered and contacted the vein wall. The authors theorized that the results indicate thrombus development due to chemical irritation is a relatively long-term process.[55] This indicates that thrombophlebitis due to higher osmolality solutions would have a greater chance of inducing thrombus formation with increased duration of exposure of the vein to the solution. Therefore, shorter in situ duration would reduce the chance of thrombophlebitis.

Bregenzer et al[6] concluded that the hazard for catheter-related complications, such as phlebitis, catheter-related infections, and mechanical complications, did not increase during prolonged catheterization compared to shorter catheterization. However, only patients requiring peripheral intravenous catheterization for 24 hours or more were enrolled in the study.

Catheter Type

Kohlhardt et al[25] randomly allocated 46 patients to receive complete intravenous nutrition by a peripheral (n = 23) or central (n = 23) route. The PIN system combined a fine-bore silicone catheter with lipid-based nutrient solutions. Problems of venous access, bacteremia, and infective phlebitis were not observed with PIN, although late-onset chemical phlebitis occurred on four occasions after a mean time of 22.8 days. The fine-bore silicone catheter PIN delivery system resulted in long-term, phlebitis-free infusions for periods similar to those of single-lumen central catheterization.

Payne-James et al[4] randomized 54 patients to have either a Vialon or a PTFE-Teflon peripheral vein cannula inserted in a vein in each forearm to observe the development of thrombophlebitis for five days. By the end of

the study, over 40 percent of both cannula types had been removed. No significant differences were found between the numbers of each cannula type removed at any time point throughout the duration of the study. Additionally, there were no significant differences in the amounts of erythema or hardness, although minimally increased swelling was observed at the mid-point of the PTFE-Teflon cannulas.

Myles et al[37] prospectively evaluated a 16-gauge bismuth oxide-Teflon cannula compared to a Vialon cannula in 200 patients. There were no differences in the incidence of thrombophlebitis between the two cannulas. May et al[31] examined several different cannulas and found severe phlebitis and line occlusion occurred more frequently in patients with a 15-cm catheter compared to a regular 5-cm cannula. They concluded mechanical trauma is an important factor in the etiology of infusion phlebitis, and can be minimized by reducing the amount of prosthetic material within the vein.

Everitt and McMahon[56] conducted a randomized, controlled study in which a standard nutritional solution was infused via 22G polyurethane catheters inserted to a length of either 5 cm or 15 cm, in order to compare the effect of catheter length on phlebitis. No significant differences were found between insertion lengths in median time to thrombophlebitis or extravasation, or in daily risk of thrombophlebitis. Survival proportions of the catheters were similar for each length at all times.

Miscellaneous

DeLuca et al[57] examined the effect of final filtration on the incidence of infusion phlebitis in a prospective, double-blind investigation. The incidence of infusion phlebitis in 146 postoperative patients was significantly reduced when an in-line, 0.45 mm membrane filter was used. The greatest reduction of infusion phlebitis was in the filter groups receiving unbuffered solutions and no set change over the 72 hours of therapy. Buffering the infusion fluid or 24-hour change of the administration set did not have any effect on reducing the incidence of phlebitis. A significant rise in white blood cell count and an increase in sedimentation rate were observed in patients receiving unfiltered fluids. The authors recommended that inline final filters should be a part of routine intravenous therapy.

De Vries et al[58] studied the effectiveness of the two most widely used skin disinfectants, alcohol 70 percent and alcoholic iodine 2 percent, in a prospective randomized trial. Phlebitis was seen twice as often in the iodine group, but failed to reach significance (p=0.18) due to the low power of the study (0.55).

Recommendations

Recommendations for the administration of out-patient, office based PIN must use the evidence available in the literature, but be applied to this specialized area that has as yet not been studied (Table 1).

Infusion osmolalities can venture high into the hyperosmolal range as long as the duration of the infusion is brief. Osmolalities of 800-1000 mOsm/L are most likely justifiable, and even higher ranges can be used if

Table 1: Recommendations for Out-Patient, Office-Based PIN

Osmolality less than 1000
Fine-bore catheters
Large antecubital vein
In-line 0.45 mm or smaller filter
Proper skin disinfection with 70% alcohol
Infusion rate of 150-330 mL/hr
Infusion rate of 1.5 to 3 hours

additives such as heparin, hydrocortisone, and transdermal glyceryl trinitrate patches are used. Dilution of the infusion to reduce the osmolality, even if it necessitates an increase in infusion rate to maintain a brief duration, is recommended.

The infusion duration in an out-patient, office-based PIN should, for practical reasons, range from 1.5 to 3 hours. The brief infusion duration serves to decrease the length of time the irritating mixture is in contact with the vein wall, decreasing the incidence of phlebitis, since chemically-induced phlebitis takes several days to occur. However, brief duration requires high infusion rates be used (150-330 mL/hour), thereby decreasing the dilution effects of the venous blood. Due to this requirement, the largest vein possible should be used, preferably those in the antecubital fossa. To minimize mechanical trauma to the vein, the smallest and shortest catheter possible to achieve the desired infusion rate should be used. In-line filtration of at least 0.45 mm should be used and the cannula should be removed at the first sign of pain or redness.

Infection risks need to be minimized through the use of standard procedures, despite the low incidence of bacteria-induced phlebitis demonstrated in the literature. Alcohol 70 percent should be used as the skin disinfectant of choice. Further prospective, randomized, controlled trials are needed to examine whether these recommendations, derived from the in-patient based PIN literature, can in fact be applied to out-patient, office-based PIN.

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