Heparin Versus Normal Saline as a Flush Solution

1Hepzibha Alexander
School of Nursing, UCSI University, Kuala Lumpur
hepzi.alexander@gmail.com

Abstract
“Heparin versus normal saline” - the search for the better flush solution began a couple of decades ago as nursing moved from a traditional practice into an Evidence-based Practice, where the best course of action is based on current and reliable evidence.

Objectives: The study seeks to critically evaluate the effectiveness of heparin on duration of catheter patency and complications associated with peripheral venous and arterial catheters, based on the principles of Evidence-Based Practice (EBP).

Methods: The electronic database of Ovid, Pub-Med, The Cochrane Library and The Cochrane Database of Systematic Reviews (CDSR) was searched using keywords containing heparin or normal saline (either singly or in combinations). The search was limited to studies carried out on human subjects only. Relevant studies were critically appraised and evidence obtained was graded according to the modified CAHTA scale.

Results: The available evidence is very inconsistent on the effectiveness of heparin over normal saline for venous catheters. However, a number of studies showed that normal saline is just as effective as and more efficacious than heparin. For arterial catheters, majority of the available data suggest that heparin saline given as a continuous flush at low doses improved catheter patency. However, heparin as an intermittent flush is ineffective. In terms of safety, the findings indicate that it might be safer to use normal saline as it does not have the risks associated with heparin. Cost analysis studies proved without any doubt that use of normal saline flush results in a significant amount of cost savings.

Conclusion: Normal Saline should be used as an alternative to heparin in intravenous catheters. Low-dose heparin (0.25U/ml) should be added to the infusate to maintain patency of arterial catheters. Extra precautionary measures must be taken when heparin therapy in instituted. Nurses and other healthcare professionals need to be reeducated on the side effects and complications of heparin therapy in order to prevent unnecessary complications and to provide safe and effective care.

Keywords: Heparin, normal saline, venous catheters, arterial catheters

1. INTRODUCTION

“Heparin Flush Versus Saline Flush” has been the major topic in discussion among the healthcare professionals for the last couple of decades. Traditionally heparin has been used (in varying doses) as a flush solution to prevent the formation of clots in intravascular devices due to its anti coagulation properties, despite the known fact that heparin can cause critical side effects such as haemorrhage, Heparin-induced Thrombocytopenia (HIT) and
hypersensitivity. With the shift of nursing from a traditional practice into an Evidence-based Practice, the debate about the effectiveness of normal saline as a flush solution for intravascular devices came into question. It was at this point that researchers started asking the important question “Do the benefits of heparin outweigh the risks?” Numerous research and clinical trials have been done to determine the effectiveness of normal saline over heparin in catheter patency and its associated complications. However, there is still a significant amount of ambiguity surrounding the issue because of heterogeneity in the studies and variability in clinical practice.

2. BACKGROUND

A. Heparin

Heparin is the oldest and still widely used substance in medical history. Heparin is an anticoagulant and works by inhibiting reactions that lead to the clotting of blood and the formation of fibrin clots both in vitro and in vivo (RxList: The Internet Drug Index, 2008). These drugs tend to prevent new clots from forming or an existing clot from enlarging. They don't dissolve a blood clot (American Heart Association, 2009).

Clinically, “heparin is effective for prevention and treatment of venous thrombosis and pulmonary embolism (PE), for prevention of mural thrombosis after myocardial infarction (MI), and for treatment of patients with unstable angina and MI.” (Hirsh, Anand, Halperin & Fuster, 2001). It is also useful in the diagnosis and treatment of acute and chronic consumptive coagulopathies (disseminated intravascular coagulation), prevention of clotting in arterial and cardiac surgery; prophylaxis and in the treatment of peripheral arterial embolism. Heparin may also be employed as an anticoagulant in blood transfusions, extracorporeal circulation, and dialysis procedures and in blood samples for laboratory purposes (RxList: The Internet Drug Index, 2008).

B. Normal Saline

Normal saline (0.9% sodium chloride), a class of intravenous (IV) fluids called crystalloids is the most widely used infusion solution in the entire world due to its isotonic concentration. It is a sterile solution of sodium chloride (table salt) in water.

Normal Saline serves a number of purposes in healthcare setting. It is used as:
1. IV therapy for severe dehydration
2. Rinse for contact lenses
3. Wound care for irrigating, cleansing and hydrating wounds
4. Nasal irrigation

3. OBJECTIVES

To critically evaluate the effectiveness of heparin on the duration of catheter patency and complications associated with peripheral venous and arterial catheters, based on the principles of Evidence-Based Practice (EBP).
4. METHODOLOGY

The electronic database of Ovid and Pub-Med was searched using the following keywords either singly or in combinations: heparin saline, normal saline, arterial catheter(s), venous catheter(s), heparin flush, saline flush, catheter patency, intravenous, intra-arterial, IV, effectiveness, efficacy, heparin versus normal saline, heparin vs normal saline, hepariniz(s)ed, non-hepariniz(s)ed, cost effectiveness, benefits, risks, complications, safety, systematic review(s). In addition the following databases were searched:

- The Cochrane Library
- The Cochrane Database of Systematic Reviews (CDSR)

The search was limited to studies carried out on human subjects only. Relevant studies were critically appraised and evidence obtained was graded using the modified Catalan Agency for Health Technology Assessment (CAHTA) scale.

5. RESULTS AND DISCUSSION

A. Venous Catheters

a. Effectiveness

Most of the available evidence was inconsistent and inconclusive largely due to heterogeneity of the studies. Certain studies looked at intermittent infusions (Lopez-Briz & Luis Garcia, 2005; Rabe, Gramann, Sons, Berna, González-Carmona, Klehr, et al, 2002; Meyer, Little, Thorp, Cohen & Yeast, 1995) while others took into account both intermittent as well as continuous infusion (Randolph, Cook, Gonzales & Andrew, 1998). The study population varied across studies and included neonates, pediatrics, adults from ICU, medical-surgical units and obstetric clients. There were significant differences in the dose, the route of administration of heparin and the outcomes reported across studies.

Shah & Shah (2008), Rabe, Gramann, Sons, Berna, González-Carmona, Klehr, et al (2002), Mudge, Fudge & Sattery (1998) and Meyer, Little, Thorp, Cohen & Yeast (1995) concluded that heparin is more effective than normal saline, in that, it prolongs the duration of catheter patency and reduces the risk of potential complications. On the other hand, other studies suggest that normal saline is significantly effective than heparin in prolonging the patency of IV catheters, reducing the possibility of drug interactions and is cost-effective (Kaneko, Iwano, Yoshida, Kosuge, Ito, Narita, et al, 2004; Paisley, Stamper, Brown, Brown & Ganong, 1997; Leighton, 1994 and Barrett & Lester, 1990). The systematic review by Lopez-Briz & Luis-Garcia (2005) supports the use of heparin, however, the authors themselves comment that the evidence is poor due to methodological limitations and more randomized clinical trials are needed to achieve conclusive results.

Other studies (Mok, Kwong & Chan, 2007; Nelson & Graves, 1998; Goode, Titler, Rakel, Ones, Kleiber, Heilskov, Kleiber, Johnson & Miller, 1998; Stephens, Haire, Tarantolo, Reed, Schmit-Pokorny, Kessinger et al, 1997; Robertson, 1994; Small et al, 1991; Ashton, Gibson & Summers, 1990; and Hamilton, Plis, Clay & Sylvan, 1988) were neutral and concluded that normal saline is just as effective as heparin.
The systematic review and meta-analysis by Randolph, Cook, Gonzales & Andrew (1998) had good methodological quality and took into consideration the heterogeneity of the studies. The authors suggest that use of heparin as intermittent flushes had no benefit over normal saline. However, continuous infusion of heparin at 1U/ml significantly reduced the risk of phlebitis, increased the duration of catheter patency and reduced infusion failure.

It is difficult to draw a conclusion as to whether heparin is better than normal saline based on the available evidence as the findings are very inconsistent. However, it is important to note that a number of studies showed that normal saline is equally effective as heparin.

b. Efficacy

Demir & Dramali (2003) and LeDuc (1997) suggest that normal saline is more efficacious than heparin for maintaining the patency of peripheral intermittent IV lines. LeDuc (1997) goes on to suggest that normal saline may very well be an effective alternative to heparin flush in the pediatric population as it prolongs the catheter patency and eliminates the risks associated with heparin.

Fuentes I Pumarola, Casademont Mercader, Colomer Plana, Cordon Bueno, Sabench Casellas, Felez Vidal et al (2007), Thamlikitkul & Indranoi (2006) and Niesen, Denise, Linda & Lynn (2003) agree that saline flush is as beneficial as heparin saline; however, normal saline flushes are not usually prescribed. Thamlikitkul and Indranoi emphasize that knowledge should be translated into actions and efforts must be made to bridge the gap between theory and practice.

From the available evidence, it can be safely concluded that normal saline is as efficacious as heparin.

c. Safety

Patient safety is always a top priority in any nursing intervention. Several studies (Demir & Dramali, 2003; Goode, Titler, Rakel, Ones, Kleiber, Small et al, 1991 and Ranze, Ranze, Magnani & Greinacher, 1991) indicate that quality of care can be enhanced by using normal saline as the flush solution as it eliminates the severe complications associated with heparin such as heparin induced thrombocytopenia (HIT), thrombus and hemorrhage. A case report by Lambert, Deneys, Pothen, Vermylen & Hermans (2006) states the condition of a 3-year old boy with Haemophilia A, who developed systemic anticoagulation as a result of regular rinsing of central venous catheter with heparin.

On the other hand, a study done among orthopedic patients post-surgery revealed a greater incidence of thrombophlebitis and suggests that the use of normal saline should be avoided in post-operative patients. Hentschel, Wiescholek, Von Lengerke, Harms, & Jorch (1999) explain that a stringent protocol of heparinization leads to a low incidence of complications potentially amenable to anticoagulation.

Although the existing data is divided, it is a well-known fact that there is always a potential of developing mild to severe complications when heparin therapy is initiated. Weighing the benefits against the risks, it would be safer to use normal saline as the flush solution.
B. Arterial Catheters

a. Effectiveness

A review of six randomized controlled trials in neonates by Barrington (1999) suggests that heparinization of the fluid infused through an umbilical artery catheter decreases the likelihood of the umbilical catheters occluding. However, heparinization of flushes without heparinizing the infusate is ineffective. Other studies (Halm, 2008; Randolph Cook, Gonzales & Andrew, 1998; Zevola, Dioso & Moggio, 1997; AACN Thunder Project, 1993 and Rais-Bahrami, Karna & Dolanski, 1990) also approve that maintaining arterial catheters with heparinized solutions prolongs the duration of catheter patency and reduces clot formation.

A randomized, double-blind, placebo-controlled trial by Del Cotillo, Grané, Llavoré, & Quintana (2008) conclude that use of heparinized solutions did not increase catheter patency but altered APTT (Activated Partial Thromboplastin Time) significantly. Hall, Whitta, Bennetts, Welman & Rawlins (2006) found a similar conclusion that heparin as a continuous flush at 3U/ml did not improve the function of arterial lines as compared with saline flush. Leighton (1994) concludes that it is practical to maintain arterial lines with normal saline as it has the same benefit as heparin without the risks associated with heparin. However, Clifton, Branson, Kelly, Dotson, Record, Phillips et al (1991) contradicts the conclusion that normal saline is beneficial. His study states that use of normal saline as a continuous flush for radial artery catheters is associated with increased frequency of catheter occlusions compared with heparin.

Lapum (2006), Kulkarni, Elsner, Ouellet & Zeldin (1994) and Peterson & Kirchhoff (1991) were neutral in their results and concluded that no significant differences were found between intravascular catheters flushed with heparinized solution and those flushed with non-heparinized solutions.

Majority of the studies mentioned above used heparin at varying doses (0.25 U/ml or 1U/ml). Studies (Barrington, 1999; Bolgiano, Subramaniam, Montanari, & Minick, 1990) done to determine the effective dose of heparin conclude that 0.25 U/ml is sufficient for maintenance of arterial catheters.

Majority of the available data suggest that heparin saline given as a continuous flush at low doses improved catheter patency. However, heparin as an intermittent flush is ineffective.

b. Efficacy

Double-blind, randomized controlled studies by De Neef, Heijboer, Van Woensel & De Haan (2002) and Rajani, Goetzman, Wennberg,Turner & Abildgaard (1979) conclude that the use of normal saline in arterial catheters is associated with an increased frequency of catheter non-patency as compared with heparinized saline.

On the contrary, Tuncali, Kuvaki, Tuncali & Capar (2005) suggested that there are no significant differences between heparinized and non-heparinized flush solutions in the maintenance of arterial catheters. He emphasized that heparin should be eliminated and saline should be used as the flush solutions as it cuts the cost and reduces the risks associated with heparin.
The available evidence is divided and inconclusive.

c. Safety

A major concern, in terms of safety of heparin flush is the alteration of APTT values (which are heparin-sensitive) and the development of Heparin-induced Thrombocytopenia (HIT). Studies done by Alzetani, Vohra & Patel (2004) and Hoste, Roels, Decruyenaere & Colardyn (2002) reveal that samples withdrawn from heparinized arterial lines cannot be relied upon as heparin significantly prolongs APTT values. Matsuo, Kusano, Wanaka, Ishihara & Oyama (2007) reports the case of a 60-year old woman on dialysis who developed acute systemic reactions with acute pulmonary embolism a few minutes after manipulation with heparin flush.

Hall, Bennetts, Whitta, Welman & Rawlins (2006) and Hentschel, Wiescholek, Von Lengerke, Harms & Jorch (1999) found contradictory results that suggest the use of heparin in normal saline as a continuous flush does not reduce platelet counts in critically ill patients. Hentschel goes on to say that a stringent protocol of heparinization leads to low incidence of complications.

Heparin is capable of causing some serious adverse effects as stated in the above evidence. Therefore, it might be safer to use normal saline as it does not have the risks associated with heparin.

C. Cost effectiveness

In this current era of economic crisis, cost-effectiveness has become a top priority for healthcare organizations as well as the patients. Several reports concluded that switching from heparin to normal saline flush cuts the cost significantly. Carlson, Honald & Tyndall (1989) shows that conversion of the entire hospital to normal saline-only flush resulted in cost savings of $ 91, 000 (RM 296,164.16). Fishman, Roberts & Hotaling (1989) in an ASHP clinical meeting presented an annual cost savings of $ 40, 000 (RM 130, 187. 91) as a result of switching from heparin to normal saline flush. Similarly, Gentry & Fudge (1990) reported a cost savings of $ 45, 000 (RM 146, 460.06). A meta-analysis of 15 studies revealed that an estimated yearly savings of $109, 100, 000 (RM 355,082,679.76) to $218, 200, 000 (RM 710,199,687.90) could be attained by using saline flush(Goode, Titler, Rakel, Ones, Kleiber, Small et al, 1991). Again, an open trial by Guharoy & McGalliard (1992) resulted in cost savings of $ 4, 100 (RM 13, 346. 29) in the first four months. LeDuc (1997) provided an estimated annual cost savings of nursing time and unit cost of solutions equaling $ 27, 594 (RM 89, 824.05). The savings per procedure was estimated to be $9. 45 (RM 30. 7617).

It can be safely concluded that the use of normal saline flush results in a significant amount of cost savings.

6. SEARCH FOR OTHER SOLUTIONS

The search for other flush solutions besides heparin and normal saline has yielded promising results. Current research shows that sodium citrate, a crystalline salt, has proven to be an effective flush solution.
A. Venous Catheters

a. Efficacy

A retrospective analysis (Grudzinski, Quinan, Kwok & Pierrato, 2007) in a haemodialysis unit converted to locking all central venous catheters with sodium citrate and compared the outcomes of the year prior and after the conversion. They concluded that sodium citrate (4%) is efficacious as heparin and offers potential advantages than heparin as it avoids exposure of patient to the risks associated with heparin.

b. Cost Effectiveness

The above-mentioned retrospective analysis (Grudzinski, Quinan, Kwok & Pierrato, 2007) also analyzed the cost implications and concluded that conversion to sodium citrate generates an annual cost savings of $861.12 per patient (based on thrice-weekly dialysis) which translates to an 85% cost reduction.

B. Arterial Catheters

a. Efficacy

A randomized, controlled trial by Branson, McCoy, Phillips & Clifton (1993) revealed that arterial catheter flush solutions containing sodium citrate (1.4 percent) are an effective and safe alternative to heparin in patients requiring peripheral arterial catheterization.

It is possible that sodium citrate may be an alternative to heparin flush. But more research needs to be done in order to explore this possibility.

b. Safety

A randomized, controlled trial (Cardinal, Allan, Pham, Hindmarsh, Jones & Delisle, 2000) was done to determine the effect of sodium citrate on acid-base balance and electrolyte measurements. The results of the study showed that sodium citrate used to maintain arterial catheters can contaminate blood samples and the result of that contamination can mimic severe hypocalcemia, metabolic acidosis, and mild hyperglycemia. The authors emphasized that failure to recognize the effects of sodium citrate on acid-base and electrolyte measurements may lead to changes in treatment that could affect patient outcome adversely.

The safety of sodium citrate in arterial catheters is still questionable. Further research is needed to provide conclusive results.

7. IMPACT ON CLINICAL DECISION-MAKING AND HEALTH OUTCOMES

There is documented evidence of health care organizations switching from the traditional practice of using heparin to the evidence-based practice of using normal saline all over the world. This is largely because normal saline does not have associated complications like heparin and it is very cost effective. There is also a positive trend towards using normal saline as a flush solution for venous catheters and using low-dose heparin infusion for arterial catheters. However, heparin is still widely used in Malaysia as a flush solution despite its well-known complications, simply because normal saline is just not prescribed. It is high
time to let go of blind traditional practices and institute protocols for using normal saline as a
flush solution for venous catheters.

In addition, a well-designed, prospective, randomized clinical trial that takes into account the
heterogeneous nature of the subject is essential to determine conclusively the effectiveness of
normal saline over heparin.

Also, further research into the effectiveness and safety of sodium citrate needs to be explored
in order to identify an effective flush solution for the future.

8. CONCLUSION

The answer to the debate “Heparin versus Normal Saline” is not completely clear. However,
certain conclusions can be drawn from the available evidence. A vast majority of studies on
venous catheters came to a neutral conclusion that normal saline is as effective as heparin and
it does not have the severe complications associated with heparin. An analysis of cost
revealed that switching to normal saline cuts the cost significantly. Therefore, weighing the
benefits against the risks, it can be concluded that normal saline is beneficial and therefore
should be used for venous catheters.

For arterial catheters, a majority of the evidence pointed to the use of low-dose heparin saline
as a continuous flush at the rate of 0.25 U/ml as more effective normal saline. However, the
complications associated with heparin, which are well-known, must be considered. In this
case, choosing to use heparin means that nurses and other healthcare professionals must be
aware of the potential side effects. Nurses should monitor the client for signs and symptoms
of hemorrhage such as petechiae, bruises, blood in stool, blood in urine, nose bleeds etc. Vital
signs need to be monitored before and after the infusion of heparin and PT APTT tests should
be regularly to detect any complications early.

Nurses must constantly keep themselves abreast of current evidence because Evidence-based
Practice is safe practice.

9. RECOMMENDATIONS

From the above findings, the following is recommended:

- Normal Saline could be used as an alternative to heparin in intravenous catheters.
- Low-dose heparin (0.25U/ml) can be added to the infusate to maintain patency of
  arterial catheters. Further research to be undertaken to determine the therapeutic dose
  for continuous infusion of heparin in arterial catheters.
- Further research is essential to determine the effectiveness and safety of sodium
citrate as a flush solution.
- Nurses and other healthcare professionals need to be reeducated on the importance of
  following an Evidence-based practice as opposed to traditional methods in order to
  provide the best possible care to the client.
10. REFERENCES


Hepzibha Alexander, born in India on February 3, 1987 completed her Bachelor of Nursing (Hons.) at UCSI University, Kuala Lumpur in 2009. She has worked part-time as a telemarketer for a financial training company, volunteered with local NGOs for community healthcare clinics and the Student Nurses' Association for the HIV awareness campaign. She is interested in all issues regarding healthcare, especially global healthcare trends, cardiac care and healthcare economics.