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An Evidence Based Recommendation for the Use of 5% Human Albumin vs. Normal Saline with Hypotension Secondary to Hypovolemia in Adult Post Operative Patients

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AN EVIDENCE BASED RECOMMENDATION FOR THE USE OF 5% HUMAN
ALBUMIN VS. NORMAL SALINE WITH HYPOTENSION SECONDARY TO
HYPOVOLEMIA IN ADULT POST OPERATIVE PATIENTS

A project submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Nursing

By

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Abstract

Problem: 5% human albumin is used very frequently in the hospital setting with hypotensive post-surgical patients. There are associated risks with the use of human albumin and it has been shown that normal saline is at least as effective in treating extreme hypotension in this patient population.

Significance: Associated risks that are present with the use of human albumin may be equal to those of the risks of whole blood transfusions. In addition weight gain and fluid retention are complications associated with the use of human albumin versus the use of normal saline. Furthermore, human albumin costs \$40.59 more than normal saline solution.

Methods: Literature review and the IOWA Model.

Results: Patients who are not at risk for post-perfusion syndrome, pulmonary hypertension, on strict intake and output regulation, or increased vascular permeability and are experiencing hypotension secondary to hypovolemia post-operatively would benefit from normal saline as a first line therapy.

Key words: hypotension, fluid resuscitation, fluid loss, hypovolemia, cost, safety, post-operative, colloid, crystalloid, human albumin, 5% albumin, normal saline, saline

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Chapter One: Introduction

Current practices of fluid resuscitation for the treatment of hypotension secondary to hypovolemia in the adult post-operative patient are inconsistent and may place the patient at risk with the chosen treatment. Despite previous evidence-based administration guideline recommendations, it was found that human albumin was inappropriately used for 57.8% of adult patients (Boldt, 2010).

Currently, hospitals lack recommendations to assist in the selection of the appropriate treatment. The chosen treatment is dependent on the surgeon's preference and is not necessarily evidenced-based (Roberts, et al., 2011). Human albumin solutions and saline solutions are used frequently in emergent and post-surgical patients to stabilize extreme hypotension and low blood pressure due to fluid loss. Human albumin solutions are more expensive than other comparative colloids and crystalloids, but the major consideration is the safety profile of the human albumin. Normal saline has been found to be at least as effective as 5% human albumin solution at treating hypotension and in turn it is a sustainable alternative to human albumin (Roberts, et al., 2011).

Through successful conclusion of this project I was able to promote the most efficacious, safe, and cost-effective evidence-based recommendation possible to the patient population. By analyzing the current research on the effect of human albumin vs. normal saline in the outcome of post-surgical patients who experience extreme

hypotensive episodes, I analyzed and utilized the evidence to develop an evidence-based recommendation for surgeons to consider. In the next chapter, I discussed the model which was used to structure my project.

Chapter Two: Model

Iowa Model

The Iowa Model of Evidence-Based Practice to Promote Quality Care is a useful model for the nurses to follow in order to know how to begin, develop, and assess evidence-based practice (Burns & Grove, 2009). This model can be used to help nurses make daily decisions in the care of their patients. The Iowa Model provides a framework allowing for all members of the healthcare team to be included in the quality change. For this reason, I chose this model. It allows the change to be a team effort and increases the likelihood of a successful implementation a successful implementation (Burns & Grove, 2009).

There are seven steps in the Iowa model (Doody, C.M, & Doody, O.,2001). The first step is to select a topic. The topic should be a trigger for needed change such as a clinical problem. Changes are necessary to keep nursing practices current. The use of the best evidence to provide effective and cost-appropriate treatment is the goal of the changing current practices. The topic should have a large amount of data and evidence in the area of need. Forming a team is the second step in the Iowa model. The team should consist of at least one person under the guidance of a committee. Team responsibilities include development, implementation, and evaluation of the EBP. (Doody, et al.,2001).

The third step is evidence retrieval. This is simply searching for the evidence necessary to address the problem of focus and then to use the evidence to recommend change the current practice. There must be sufficient data to support the propose change.

A paucity in the literature would indicate the topic is not appropriate for an evidence-based project, but for a research thesis. Grading the evidence is the fourth step and allows the person developing the project to evaluate the effectiveness, appropriateness, and the feasibility of an appropriate outcome (Doody, et al.,2001).

The fifth step is to develop the evidence-based recommendation standard: “This sets the standard of practice guidelines, assessments, actions, and treatment as required” (Doody, et al.,2001). The recommendation that I developed included both the pros and cons found in the literature. The standard should be supported by the pros, but caregivers need to be aware of the limitations of the treatment to provide efficient care.

The sixth step is to implement the recommendation. This step requires interaction between all levels of care. Management and direct care employees need to be trained with the new practice and the new recommendation by a member of the committee. If workers understand the benefits of this change, they will be more likely to comply with the new recommendation (Doody, et al.,2001). The seventh and final step is to evaluate the project’s level of change and value. Ultimately this step is used to see how well the project was implemented and to achieve a solution to the problem trigger (Burns & Grove, 2009).

Chapter Three: Framework

Synthesis of Data Retrieval

To complete the review of literature, I began on the Cedarville University Centennial Library's website. I used the "multiple databases" tab to select the following databases: CINAHL Plus with Full Text, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. The advanced search tab allowed me to narrow down my findings. I did not select the option for "results with full text" as this may have excluded articles that could be requested from other libraries.

I also selected the "peer reviewed" and "evidenced-based" article options, and the initial timeline was set to gather articles from within the last five years. The timeline eventually expanded to 10 years, with the exception of one article. This article was repeatedly listed as a reference in current articles, indicating its validity for current research. Once I had reviewed the articles, I checked their references for additional articles and searched for those which were relevant.

Search Terminologies

I used the following terms to narrow the evidence findings: "hypotension", "low blood pressure", "post-surgical", "fluid loss", "hypovolemia", "cost", "treatment", "therapy", "illness", "guidelines" and "adverse effects" in combination with either "human albumin" or "normal saline". I also used the following as substitute terms for normal saline: "saline", "0.9% saline", and "crystalloid". For "5% human albumin", I

substituted the terms “human albumin”, “albumin”, “5% albumin” and “colloid”. Not every search needed to include human albumin and normal saline together. I was able to gather research data that was related to one or the other and gain insightful data about that solution.

Inclusion & Exclusion Data

The inclusion data is very broad. The patients must be hospitalized, living, adult humans, of any race or any gender. The unit in which the recommendation was presented was an adult cardio-thoracic care unit. The patient population consisted of postoperative adults and included a high level of patients for whom strict intake and output regulation was monitored. Currently, 5% human albumin is given for hypotension secondary to hypovolemia for most patients. While this recommendation is based on the surgeon’s preference, patients recovering from a coronary artery bypass graft may have two bottles of 5% human albumin for a total of 500 ml per standing order to treat mean arterial pressures lesser than sixty mm Hg or for urine output less than thirty mL over one hour. Articles were considered from all countries, as inclusion of only articles from the United States would have considerably limited the search results. The articles needed to include the administration of 5% human albumin and/or normal saline to a patient. I considered articles that included either normal saline or 5% human albumin even if the title did not mention a hypotensive situation. As a result, I was able to review a broader base of literature.

I excluded articles unrelated to in-patient related fluid replacement therapy. I also excluded articles that were not published or updated in the last ten years, except for the article that was repeatedly referenced by current articles. If the article did not use adults

only, the research was excluded. I did not initially account for sample size, but I considered its impact during the evaluation of each article.

Ethical Considerations

I did not implement research on human subjects, and I did not need approval from the Institutional Review Board (IRB). This final outcome of this evidenced-based research project was based upon completed research to date. I did not actively collect data with human participants.

Any negative effects regarding use of saline over human albumin or vice versa that led to a negative outcome would have been an ethical dilemma. If the outcome of the literature review had resulted in a possible negative outcome for the patient, I would not have recommended that specific replacement therapy.

Specific Timeline

I needed to finish retrieving and grading evidence by March 14, 2013. I needed to develop an evidence-based recommendation or recommendation and present it to my unit Nurse Educator and stakeholder, Dawn Myers, by June 14, 2013. I met with one of the hospital's main cardiothoracic surgeon's, Dr. Pavlina, MD on August 2, 2013. I met with my Evidence Based Project Committee intermittently throughout this timeline.

Evidence Based Project Committee

Amy Voris, DNP, CNS, AOCN, Rachel Parrill, PhD, APHN-BC, Dawn Myers, MSN, RN were on the committee of my evidenced- based project. They were a great reference to facilitate the growth of my project and, in the end, successfully implement my evidenced-based recommendation. In the subsequent chapter, I have outlined the results of the literature review.

Chapter Four: Literature Review & Results

Methodology

For this review of literature, I accessed the following databases: Cedarville University CINAHL Plus with Full Text, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. I used the following key words to research related study reports, articles, and research studies:” hypotension”, “fluid resuscitation”, “fluid loss”, “hypovolemia”, “cost”, “safety”, “post-operative”, “colloid”, “crystalloid”, “human albumin”, “5% albumin”, “normal saline”, and “saline”. The time frame of the literature search was about eight days, and twenty articles were found. Two articles were not accessible through inter-library loan, and five articles were excluded from the review. I have outlined inclusion and exclusion of articles in the next section.

Inclusion & Exclusion Data

Inclusion. Articles were required to have included patients that were post-surgical. Fluid resuscitation was also required as a treatment for hypotension. I preferred studies that used either normal saline or 5% human albumin, but I considered all crystalloids and colloids used for a more general outcome regarding the overall classification. I focused on trends in cost, efficacy, and safety within the classes.

I also included studies that involved some but not all post-surgical patients were included. The outcome of the study, however, needs to reflect the difference in risk between post-surgical and non-post surgical patients in regard to fluid resuscitation. I

included studies that used human albumin and normal saline on non-surgical patients only if information regarding cost or safety (i.e., blood borne diseases) was included.

Exclusion. I excluded one article that included fluid resuscitation of a dialysis patient with no presence of a recent surgery. I excluded four articles due to their focus on the neonatal population.

Thirteen articles were reviewed, analyzed, and graded on their level of evidence based on the Levels of Evidence for Primary Research Question criteria (Rahman & Pukui, 2002). The grading criteria can be found in Appendix A. The results of the analysis are listed below and are specified by author, year published, title, design of the research, specific solutions compared, and the level of evidence.

Review of Literature

Fluid resuscitation is a common first-line treatment for hypotension related to hypovolemia and results in a “rapid increase of cardiac output and tissue oxygenation” (Trof, Sukul, Twusj, Girbes, & Groeneveld, 2010, p 697). Crystalloids and colloids are the two types of fluid available. The patient’s specific necessities are the determinant of which type of fluid is provided.

Crystalloids are fluids that are given to maintain electrolyte and fluid equilibrium (Ignatavicius, D., & Workman, L, 2006). Ringer’s lactate and normal saline are common crystalloids. Ringer’s lactate is a mixture of potassium, sodium, chloride, calcium, and lactate that is dissolved in water. This solution is isotonic and is appropriate to be used to expand volumes, and the added lactate is appropriate to buffer out acidosis. Normal saline is a mixture of 0.9% sodium chloride and water. It is good for fluid replacement to increase the intravascular volume. Crystalloids are good options for fluid

replacement/expansion when there is no loss of red blood cells (Ignatavicius, et al., 2006).

Colloids are fluids that contain protein and are given to reestablish osmotic pressure and expand the intravascular fluid volume (Ignatavicius, et al., 2006). Colloids include whole blood, packed red blood cells (PRBCs), plasma, plasma fractions, and synthetic plasma expanders. Human albumin is a plasma protein fraction. Plasma protein fractions and synthetic plasma expanders are given when hemoglobin and hematocrit are within normal ranges and creates the benefit of an increase in osmotic pressure (Ignatavicius, et al., 2006). A plasma protein fraction, such as human albumin 5%, is not able to improve the oxygen-carrying function as whole blood or PRBCs can (Ignatavicius, et al., 2006).

Efficacy, safety, and cost are analyzed in the subsequent sections. The summary and limitations to the studies are successive to efficacy, safety, and cost with the literature reviewed referenced in Table 1 and Table 2 in the conclusion of this section. Table 1 includes the literature reviewed that supports the use of Human Albumin in the adult post-operative patient who is experiencing hypotension secondary to hypovolemia. Table 2 includes the literature reviewed that supports the use of Normal Saline in the adult post-operative patient who is experiencing hypotension secondary to hypovolemia.

Efficacy. Efficacy is defined as “the power to produce an effect” (Merriam-Webster). The chosen treatment must have a positive effect for the patient and be at least as or more efficient than alternative therapies. The effect of human albumin or normal saline must create an increase of blood pressure in order to correct the hypotension secondary to hypovolemia.

The SAFE Study compared mortality rates of patients between those who received 4% human albumin versus normal saline. These authors reported that human albumin and normal saline resulted in similar outcomes at 28 days for ICU patients. (Finfer, S., Bellomo, R., Boyce, N., French, J., Myburgh, J., & Norton, R. (The SAFE Study Investigators), 2004). Although, these researchers used 4% albumin and not 5% albumin this is not a significant variation. These researchers further report that 1) Net intake of normal saline was not significantly greater than that of human albumin, 2) there was no difference between groups on packed red blood cell use, and 3) central venous pressures were higher in the human albumin group indicating a higher amount of intravascular fluid. (Finfer, et al, 2004). This data supports that normal saline may be as effective as human albumin for the treatment of hypotension secondary to hypovolemia.

When monitoring the hemodynamic variables of the post-op patient, 5% human albumin has been found to have a greater volume expanding effect and a greater increase in the cardiac index when compared to normal saline up to a maximum infusion of 1800ml (Verheij, J., Van Lingen, A., Beishuizen, A., Christiaans, H., De Jong, J., Girbes, A., Groeneveld, A., 2006). Central Venous Pressures were increased by both solutions, but normal saline was less effective than human albumin. (Verheij, et al., 2006).

Kruer and Ensor (2012) discussed the importance of the colloid osmotic pressure (COP) and the length of time that the solution is retained in the intravascular system. The safety of the patient may be considered in the length of efficacy of the solution. The volume expanding properties of colloids remain effective for up to twenty four hours while the maximum benefit of crystalloids is four hours (Kruer et al., 2012).

In post-operative patients, especially cardiac bypass patients, the risk for post-perfusion syndrome (PPS) is high. Post perfusion syndrome causes a shift in the intravascular fluid due to the inflammatory response prompted by the surgery (Kruer et al., 2012). The histological changes show engorgement of the pulmonary vascular bed, micro-atelectasis and interstitial and alveolar hemorrhage. “Renal insufficiency, neurologic changes and hemorrhagic diathesis are additional indications of postperfusion syndrome” (Stoutenbeek, C., & Oudemans-van Straaten, H., 1990, p. 378). Use of a crystalloid would only exacerbate this syndrome and result in excessive fluid in the interstitial space. Patients at risk for third spacing benefitted from human albumin as the need for blood transfusion was decreased (Diehl-Oplinger, L., & Kaminski, M. F. (2004). Colloids, such as 5% human albumin, helped to maintain the colloid oncotic pressure and decrease the chance of hypovolemia due to fluid shifting (Kruer et al., 2012).

In contrast, findings from Devlin & Berletta (2005) were that crystalloids have been found to be more effective at volume expansion of intravascular and the interstitium and to have a more rapid equilibrium than when compared to colloids. These results argue that the use of a crystalloid results in a lower risk for pulmonary edema and improving overall organ function. Colloids help to sustain and return the volume and blood flow while normal saline and other crystalloids lower the concentration of the plasma. A lower COP results in a diminished length of time that the volume is retained in the intravascular system and is shifted into the interstitium (Trof, R., Sukul, S., Twisk, J., Girbes, A., & Groeneveld, A., 2010). This would theoretically result in more volumes of a crystalloid be given. However, the Saline versus Albumin Fluid Evaluation Study (SAFE) study mentioned above was only a ratio of infused human albumin vs. normal

saline of 1:1.4. Mean arterial pressures responded similarly with the treatment of human albumin and saline. This led to inconclusive evidenced-based findings (Finfer, et al.,2004).

In distinction to the findings of the SAFE study, crystalloid solutions are more likely to result in fluid overload because they are more quickly shifted into the interstitium. According to Verheij, et al. (2006) there are conflicting studies about the ratio of colloid to crystalloid needed. Verheij et al (2006) illuminated that cardiac and vascular patients were not included in the SAFE study and that “the retention of albumin is greater than that of saline after cardiac surgery, as inferred from measurements of plasma and extravascular fluid volumes” (p. 1036). This highlights that the conclusions found in the SAFE study are not applicable to patients who have undergone cardiac or vascular surgeries as the research has not been completed to support them.

Safety. Albumin is a nonsynthetic solution and has been found to increase risk for infections and allergic reaction (Kruer et al., 2012). Andrews (2011) outlined that human albumin carries“...cost implications as well as the potential for transmission of blood-borne viral disease such as Creutzfeldt-Jakob Disease (CJD)” (p 136). Human albumin is a blood protein and carries the risk for immune hypersensitivity, including anaphylactic shock, viral disease transmission (HIV/AIDS, Hepatitis, etc.), prion disease transmission, and possible increased edema formation once it is present in the interstitium (Robert & Bratton, 2008; Fortin, Bassett, & Musini, 2010). Robert & Bratton clarify that prion diseases and transmissible spongiform encephalopathy are always fatal (2008).

In difference, many clinicians have thought that human albumin administration could reduce mortality in hypovolemic patients (Perel, P., & Roberts, I., 2012; Roberts,

Blackhall, Bunn, & Schierhout, 2011). Vincent, Navickis, & Wilkes (2004) argued that the use of human albumin reduced morbidity in critically ill patients. In another study, 5% human albumin did reduce mortality among cardiac surgery patients when compared to crystalloid-only resuscitation (Kruer et al., 2012).

The average infusion ratio for human albumin to normal saline was 1:1.4. Despite this ration, Perel (2012) stated that the risk of fluid overload of the patient was also no longer a risk when compared to normal saline (p 5). Perel (2012) affirmed that the use of human albumin over normal saline was not justifiable as human albumin does not increase survival rate, there are additional risks compared to normal saline, and there is a significant cost increase with human albumin.

Cost. In addition to safety and efficacy the expense of the solutions is a significant factor when considering the appropriate use of human albumin versus normal saline (Roberts et al., 2008; Talasaz, A., Jahangard-Rafsanjani, Z., Ziaie, S., Fahimi, F., 2012). The national average cost of one 250ml vial of 5% human albumin is \$41.00 (FFF Enterprises, 2011). The cost of one 250ml bag of 0.9% normal saline is \$1.30 (PMI, 2012). At this cost ratio, over 31 bags of 0.9% normal saline could be purchased and to provide patient care for the cost of one 250ml vial of 5% human albumin. Kettering Medical Center Network purchases the 250 ml 5% human albumin vials at \$36.00 per vial and the 250 mL bags of normal saline for \$25.06 per case of 36 bags (Michelini, 2013). At this cost ratio, over 51 bags of 0.9% normal saline could be purchased for the cost of one 250ml vial of 5% human albumin.

Talasaz et al (2012) concluded that albumin was a costly treatment that was being used improperly. The researchers who conducted the SAFE Study indicated that the

decision to use human albumin versus normal saline should take into consideration the providers reference, cost, safety, and the individual needs of the patient (Finfer et al. 2004). This limits the ability to have a fixed recommendation. There must be a margin for critical thinking and the best evidence practice for the individual needs of the patient.

Summary. To maximize the efficacy of the solutions used. Talasaz, et al (2012) attempted to correlate the American Society of Hospital Pharmacist (ASHP) recommendation with the relevance of human albumin usage. The study failed to correlate albumin use with decreasing mortality rates, time in the hospital, length of time needed on mechanical ventilation, or renal replacement therapies (Pettila & Ruokonen, 2005; Finfer, et al., 2004) Intensive care settings include most of the appropriate situations for human albumin including but not limited to: hypervolemia, cardiac surgery, acute respiratory distress syndrome (ARDS), organ transplant, and cerebral ischemia patients (Talasaz, A., et al., 2012, 85-86).

Limitations. The SAFE study, which is the basis of many current fluid resuscitation recommendations and research reviews was a very large study with approximately 7,000 patients, though it excluded cardiac and vascular patients (Verheij, et al., 2006). This excludes a wide span of the patient population that is administered human albumin on a daily basis. There are a significant number of studies on the efficacy and safety of human albumin versus normal saline but they have resulted in mixed conclusions and with mostly small sample sizes and incomplete patient populations (Devlin and Barletta, 2005).

Devlin, et al. was graded at a Level II of evidence and may result in a recommendation of fair support of evidence. The Safe study written by Finfer, et al and

the research completed by Verheij, et al. are graded as a Level I of evidence. While these are both strong pieces of research they would separately be graded as an A or as being a good recommendation that is supported. With conflicting or inconsistent research to argue their points a recommendation of B or fair support of a recommendation would be given. However, both articles are clear that the patient population and specific needs should be analyzed prior to treatment. There is not a gold standard to eliminate the need for individualization of care. Critical thinking and judgment should be used to develop the best plan possible. For generalization purposes and when not focusing on one specific patient population, normal saline can be used as the guideline recommendation as evidenced by the SAFE study (Finfer, et al, 2004). This would be applicable to an A or of good recommendation quality.

Both Level I and Level II articles bear mixed conclusions. The SAFE study specifically outlined that if the patient does not fit generality to the study, i.e. cardiac or vascular complications, the treatment choice should rely on outlying factors: “According to the current state of knowledge, factors that may influence the choice of resuscitation fluid for a critically ill patient include the individual clinician’s preference, the tolerability of the treatment, its safety, and its cost” (Finfer, et al., 2004). This limits the standardization of the recommendation of use of human albumin versus normal saline.

Evidenced Based Clinical Recommendations

Patients who are experiencing hypotension secondary to hypovolemia post-operatively, are not on strict intake and output regulation, and are not at risk for post-perfusion syndrome, pulmonary hypertension, or increased vascular permeability would benefit from receiving normal saline as a first line therapy. 5% human albumin would

provide minimal benefit for these patients and risks associated with it would not be justified. If the normal saline has failed to correct the hypotension, human albumin may be used. This is a grade B recommendation. The levels of evidence presented are I and III. This recommendation includes multiple meta-analyses but does not consist of a randomized control trial or a non-randomized control trial. The strength of this recommendation is of good scientific evidence.

Patients, who are at risk for the conditions listed above or are on strict intake and output regulation, would benefit from receiving 5% human albumin as appropriate to the patient's specific needs in an effort to reduce the adverse effects of an increased vascular permeability. Upon further research studies that include patients at risk for post-perfusion syndrome, pulmonary hypertension, or increased vascular permeability with the post-operative cardiac complicated background this conclusion may be manipulated. Current research data suggests that there are no negative effects to the administration of human albumin versus normal saline when the use is appropriately indicated. This is a grade A recommendation. The Levels of Evidence presented are I, II & III and includes three randomized control trials. The strength of this recommendation is of strong scientific evidence. The next chapter will express the potential impact of these recommendations and how they are perceived upon presentation.

Literature Reviewed

Table 1 Literature reviewed which support the use of Human Albumin in the adult post-operative patient who is experiencing hypotension secondary to hypovolemia.				
Authors & Year published	Title	Design	Specific Solutions Compared	Level of Evidence
Devlin & Barletta 2005	Albumin for fluid resuscitation: Implications of the saline versus albumin fluid evaluation.	Systematic Review	0.9 Normal Saline, Lactated Ringers, Hetastarch, albumin, blood products	Level II
Diehl-Oplinger & Kaminiski 2004	Choosing the right fluid to counter.	Case Series	0.9 Normal Saline, 0.45% Saline, Sodium Chloride (3&5%) D ₅ W, Lactated Ringers, Dextrose Solutions (20%,40%,50%,60%,70%), Human Albumin 5% & 25%	Level IV
Finfer, Bellomo, Boyce, French, Myburgh & Norton 2004	A comparison of albumin and saline for fluid resuscitation in the intensive care unit.	Randomized Control Trial	Normal Saline, 4% Human Albumin	Level I
Kruer & Ensor 2012	Colloids in the intensive care unit.	Systematic Review	Normal saline 0.9%, Lactated Ringers, Gelatin 4%, Hydroxyethyl starch 6%, Albumin 5%, Dextran.	Level II

Verheij, Lingen, Beishuizen, Christiaans, Jong, Girbes, Wisselink, Rauwerda, Huybregts, & Groeneveld 2006	Cardiac response is greater for colloid than saline fluid loading after cardiac or vascular surgery.	Single-centre, single blinded, randomized clinical trial	Saline 0.9%, Gelatin 4%, Hydroxyethyl starch 6%, Albumin 5%	Level I
Trof, Sukul, Twish, Girbes, & Groeneveld 2010	Greater cardiac response of colloid than saline fluid loading in septic and non-septic critically ill patients with clinical hypovolemia.	Single-centre, single blinded, randomized clinical trial	Saline 0.9%, Gelatin 4%, Hydroxyethyl starch 6%, Albumin 5%	Level I
Talasaz, Jahangard-Rafsanjani, Ziaie, & Fahimi 2012	Evaluation of the pattern of human albumin utilization at a university hospital.	Retrospective Comparative Study	Human Albumin	Level III
Roberts & Bratton 1998	Colloid volume expanders: Problems, pitfalls, and possibilities.	Systematic Review	Human Albumin 5% & 25%, Dextran 40 & 70, Gelatin 4%, Hetastarch, Pentastrach	Level II

Table 2 Literature reviewed which support the use of Normal Saline in the adult post-operative patient who is experiencing hypotension secondary to hypovolemia.				
Authors & Year published	Title	Design	Specific Solutions Compared	Level of Evidence
Roberts, Blackhall, Alderson, Bunn, Schierhout 2011	Human albumin solution for resuscitation and volume expansion in critically ill patients.	Meta-analysis Randomized controlled trials	Human Albumin, Lactated Ringers, Normal Saline, hydroxyethyl starch	Level I
Vincent, Navickis, Wilkes 2004	Morbidity in hospitalized patients receiving human albumin: a meta-analysis of randomized, controlled trials.	Meta-analysis randomized control trials	Human Albumin, 0.9 Normal Saline, Lactated Ringers	Level I
Perel & Roberts 2012	Colloids versus crystalloids for fluid resuscitation in critically ill children.	Systematic Review	Normal Saline, Gelatin Hydroxyethyl Starch, Human Albumin	Level I
Petillia & Ruokonen 2005	Albumin has no benefit over saline in the critically ill.	Systematic Review	Normal Saline, 4% Human Albumin	Level I
Andrews 2011	Cochrane Nursing Care Field: Human albumin for intra-dialytic hypotension in haemodialysis patients	Systematic Review	Saline, Human albumin, Gelatin, Starches	Level III

Chapter 5: Discussion

Implementation of Recommendations

I presented the evidence-based recommendations from the literature review to the Cardio-Thoracic Care Unit (CTCU) at Kettering Medical Center on June 11, 2013. My audience included staff nurses and the Unit Educator. The presentation was completed with a poster session. I provided handouts that included the “Literature Reviewed” outlined in tables 1 and 2, the evidenced based recommendations, Appendix A, Appendix B, and references.

The audience was concerned about articles that supported normal saline in the use for all patients. The concern was that the generalizability of the normal saline might not have been studied enough in depth for all patient types. Their concerns were eased by the recommendations, as they specifically mention that patients who are experiencing hypotension secondary to hypovolemia post-operatively, are on strict intake and output regulation, and are at risk for post-perfusion syndrome, pulmonary hypertension, or increased vascular permeability should receive 5% human albumin in place of normal saline. Cost was not important to the audience as they felt their personal experience with the effectiveness of 5% human albumin warrants the increased price. Overall, the intended audience was pleased with the evidence-based recommendation and recommendations that were presented.

The next step to implement this recommendation in CTCU was to familiarize the staff and physicians with the recommendation and to encourage the recommendations be considered for every patient receiving fluid replacement therapy. I met with Dr. Pavlina on August 2, 2013. Dr. Pavlina showed genuine interest in the topic. He currently favors 5% human albumin for fluid replacement in his patients whom need volume replacement secondary to hypovolemia. He took the project handout and is going to read further into this project. It will be my next step to follow up with his outlook of the recommendations and further implement them into common practice into the CTCU.

Implications of Recommendations

The recommendation I presented to the CTCU would also be beneficial to nursing and medical staff in the Cardiac Intensive Care Unit, surgical and cardiac step-down units, and the Post-Anesthesia Care Unit at Kettering Medical Center and other regional area hospitals. These are units that provide care to post-surgery adult patients that experience hypotension secondary to hypovolemia. The implementation of the recommendations in additional units could result in decreased unnecessary spending, increased efficacy of the treatment, and increased safety of the patient population. The extensive amount of research that was readily available indicates that this is an important practice consideration worldwide and should not be limited to one patient setting. All applicable units, which provide fluid replacement therapy, would benefit from these recommendations.

Further Research & Practice

Choosing the correct therapy for each patient's condition is an art form. We must be able to use our critical thinking skills to select the best possible therapy for our

patients. Research reviews, research studies, and meta-analyses allow us to see a more diverse picture and choose the correct option for the dilemma at hand. The reviews and articles that have been reviewed have similar content but conflicting conclusions. This is a result of limited patient populations and a need for further research.

The use of normal saline in post-operative, trauma, hypovolemic, ARDS, dialysis, and most other conditions is preferred over the use of 5% human albumin. Reviews that failed to include patients of cardiac or vascular nature are not able to defend the use of normal saline for these patients, as they can't deflect the arguments of increased capillary permeability with an increase of fluid shift with appropriate hemodynamic stability data. Researchers must complete more studies that use a wide range of patient conditions, including cardiac compromised patients, to determine the efficacy of 5% human albumin compared to normal saline. This would increase the probability of having a more generalizable recommendation.

Cost was only a factor for measurement in very few studies and the significance of cost difference is only an added bonus for the use of normal saline. If there are added benefits for the use of human albumin such as decreased fluid intake, decreased mortality, and increased cardiac output, then healthcare workers should not hesitate to use human albumin. Cost of the use of human albumin and the reimbursement value should be analyzed in future reviews.

In conclusion, the successfully presented recommendation is an evidenced-based practice. Health care providers must realize that it will be important for them to utilize evidence-based practice. Two recommendations were outlined in this project and they allowed for the contexts of the patient to determine the correct therapy. This individuality

of the generalized recommendations allows for the efficacious, safe, and cost-effective care patients deserve.

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APPENDIX A

Table 3 Levels of Evidence for Primary Research Question				
	Therapeutic Studies:	Prognostic Studies:	Diagnostic Studies:	Economic and Decision Analyses:
	Investigating the results of treatment	Investigating the effect of a patient characteristic on the outcome of disease	Investigating a diagnostic test	Developing an economic or decision model
Level I	<ul style="list-style-type: none"> - High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals -Systematic Review² of Level I RCTs (and study results were homogenous³) 	<ul style="list-style-type: none"> -High quality prospective study⁴ (all patients were enrolled at the same point in their disease with > 80% follow-up of enrolled patients) -Systematic review² of Level I studies 	<ul style="list-style-type: none"> - Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference “gold” standard) -Systematic review² of Level I studies 	<ul style="list-style-type: none"> - Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses - Systematic review² of Level I studies
Level II	<ul style="list-style-type: none"> -Lesser quality RCT (e.g. < 80% follow-up, no blinding, or improper randomization) 	<ul style="list-style-type: none"> -Retrospective⁶ study- Untreated controls from an RCT - Lesser quality prospective study 	<ul style="list-style-type: none"> -Development of diagnostic criteria on consecutive patients (with universally applied reference 	<ul style="list-style-type: none"> - Sensible costs and alternatives; values obtained from limited studies; with multiway

	-Prospective ⁴ comparative study ⁵ -Systematic review ² of Level II studies or Level I studies with inconsistent results	(e.g., patients enrolled at different points in their disease or <80% follow-up). - Systematic review ² of Level II studies	“gold” standard) - Systematic review ² of Level II studies	sensitivity analyses - Systematic review ² of Level II studies
Level III	- Case control study ⁷ -Retrospective ⁶ comparative study ⁵ -Systematic review ² of Level III studies	- Case control study ⁷	- Study of non-consecutive patients; without consistently applied reference “gold” standard - Systematic review ² of Level III studies	- Analyses based on limited alternatives and costs; and poor estimates - Systematic review ² of Level III studies
Level IV	-Case Series ⁸	-Case Series	- Case-control study - Poor reference standard	- Analyses with no sensitivity analyses
Level V	-Expert Opinion	-Expert Opinion	-Expert Opinion	-Expert Opinion

1. A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.

2. A combination of results from two or more prior studies.

3. Studies provided consistent results.

4. Study was started before the first patient enrolled.

5. Patients treated one way (e.g. cemented hip arthroplasty) compared with a group of patients treated in another way (e.g. uncemented hip arthroplasty) at the same institution.

6. The study was started after the first patient enrolled.

7. Patients identified for the study based on their outcome, called "cases"; e.g. failed total arthroplasty, are compared to those who did not have outcome, called "controls"; e.g. successful total hip

arthroplasty.

8. Patients treated one way with no comparison group of patients treated in another way.

(Rahman & Pukui, 2002)

APPENDIX B

Table 4 Evidence-based validated grading rationale	
Level of Evidence Grade	Criteria
A (Strong Scientific Evidence)	Statistically significant evidence of benefit from >2 properly randomized trials (RCTs), OR evidence from one properly conducted RCT AND one properly conducted meta-analysis, OR evidence from multiple RCTs with a clear majority of the properly conducted trials showing statistically significant evidence of benefit AND with supporting evidence in basic science, animal studies, or theory.
B (Good Scientific Evidence)	Statistically significant evidence of benefit from 1-2 properly randomized trials, OR evidence of benefit from >1 properly conducted meta-analysis OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND with supporting evidence in basic science, animal studies, or theory. This grade applies to situations in which a well designed randomized controlled trial reports negative results but stands in contrast to the positive efficacy results of multiple other less well designed trials or a well designed meta-analysis, while awaiting confirmatory evidence from an additional well designed randomized controlled trial.
C (Unclear or Conflicting Scientific Evidence)	Evidence of benefit from >1 small RCT(s) without adequate size, power, statistical significance, or quality of design by objective criteria,* OR conflicting evidence from multiple RCTs without a clear majority of the properly conducted trials showing evidence of benefit or ineffectiveness, OR evidence of benefit from >1 cohort/case-control/non-randomized trials AND without supporting evidence in basic science, animal studies,

	or theory, OR evidence of efficacy only from basic science, animal studies, or theory.
D (Fair Negative Scientific Evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from cohort/case-control/non-randomized trials, AND evidence in basic science, animal studies, or theory suggesting a lack of benefit. This grade also applies to situations in which >1 well designed randomized controlled trial reports negative results, notwithstanding the existence of positive efficacy results reported from other less well designed trials or a meta-analysis. (Note: if there is >1 negative randomized controlled trials that are well designed and highly compelling, this will result in a grade of "F" notwithstanding positive results from other less well designed studies.)
F (Strong Negative Scientific Evidence)	Statistically significant negative evidence (i.e., lack of evidence of benefit) from >1 properly randomized adequately powered trial(s) of high-quality design by objective criteria.*
Lack of Evidence†	Unable to evaluate efficacy due to lack of adequate available human data.

* Objective criteria are derived from validated instruments for evaluating study quality, including the 5-point scale developed by Jadad et al., in which a score below 4 is considered to indicate lesser quality methodologically (Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996; 17[1]:1-12).

† Listed separately in monographs in the "Historical or Theoretical Uses which Lack Sufficient Evidence" section.

(Natural Standard, 2010)

