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Sepsis Bundled Care - An Early Goal Directed Therapy Application Study

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SEPSIS BUNDLED CARE

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Introduction

Septicemia is a severe pathologic condition that arises when a source of infection

becomes systemic – finding its way to multiple organ systems via the blood. It is clinically

defined by the presence of two or more systemic inflammatory response syndrome (SIRS)

criteria accompanied by suspected infection or infection (Francis, Rich, Williamson, & Peterson,

2010). Patients presenting with sepsis or septic shock progress rather quickly to serious states,

and if left untreated, may rapidly progress to death. Even with treatment, it is estimated mortality

rates for patients with severe sepsis are between 30% and 50% (Stoneking, Denninghoff, Deluca,

Keim, & Munger, 2011). The severity of this condition makes it apparent that it is a major

disease process facing our healthcare system. Over 750,000 new cases of sepsis and septic shock

present each year in the United States accounting for 215,000 deaths annually or 9.3% of all

deaths in the United States yearly (Stoneking et al., 2011).

Given the above facts, it is surprising to learn that septic shock has been recognized

since the earliest days of modern medicine (Puskarish, 2012). Only in recent times, however, has

the importance of early recognition and treatment of sepsis emerged. In 2001, a landmark study

in the treatment of sepsis was released in which researchers were able to reduce the mortality rate

due to sepsis by 16% using a form of bundled care called early goal directed therapy (EGDT)

created by researchers Rivers et. al. (Vorwerk & Coats, 2011). Patient care bundles consist of "a

set of interventions or processes of care distilled from evidence-based practice guidelines that

when implemented as a group, provide a more robust picture of the quality of care provided"

(Thomas, 2007, p. 1211). Thus, bundled care sets are based upon scientifically sound

interventions, with a cohesive shared focus, and directly relatable to metrics of quality of care.

The key to bundled care sets that differentiate them from typical care guidelines and protocols

lies in their comprehensive nature. Their purposive effects are gathered not only from each individual intervention, but the additive and interactive effects of using interventions *en masse* (Puskarich, 2012). In the case of sepsis, this care bundle took the form of Rivers's EGDT, which emphasized early recognition and treatment of sepsis. In fact, Rivers's EGDT was so successful that the EGDT concept was adopted by the Surviving Sepsis Campaign (SSC), an international cooperation of the world's leading organizations dealing with sepsis. The aim of the SSC is to improve the diagnosis, management, and survival of patients with sepsis. In 2004, they released guidelines for hospitals to base their care bundles upon, with the express goal of decreasing sepsis mortality by 25% by the year 2009 (Francis et al., 2010).

Since the SSC's formation, several studies have shown markedly improved outcomes with the use of emergency department (ED) based sepsis protocols. Using EGDT guidelines has allowed clear identification and quick treatment of sepsis to improve patient outcomes and mortality rates (Casserly et al., 2011; Francis et al., 2010; Larsen, Mecham, Greenberg, 2011; Patel, Roderman, Gehrig, Saad, & Bartek, 2010; Puskarish et al., 2011; Sweet et al., 2010; Uusitalo-Seppal et al., 2011).

Despite the evidence of the effectiveness of EGDT in reducing morbidity and mortality, a survey given to physicians at 30 academic tertiary care EDs, revealed only 7% of clinicians used EGDT (Stoneking et al., 2011). Additionally only one study conducted by Casserly and coworkers (2011) has been published in which EGDT care bundle was incorporated into the care of septic patients in the intensive care unit (ICU). Casserly's study created a collaborative approach in which most critically ill patients with sepsis were transferred from the ED to the ICU as quickly as possible to receive intensive EGDT bundled care as soon as possible. Their data suggests "the use of a collaborative protocol for sepsis intervention may decrease the time to

initiation of resuscitation for patients admitted to the ED with severe sepsis and decrease the time to transfer to the ICU." (Casserly et al., 2011)

Another very important and pertinent factor affecting all health care is cost. Many healthcare facilities are resistant to changes in care that increase cost when the trend nationally is to reduce costs as much as possible. A study by Jones et al (2011) found that the use of an EGDT increases direct hospital cost by $7028 per patient. But after performing a net monetary benefit analysis the researchers found with a 98% probability that EGDT was cost effective (Jones, 2011). This suggests that while initial costs of EGDT implementation are higher, the long term and overall benefits actually outweigh that cost in value.

An ad hoc committee of specialists at the study hospital developed the Sepsis Powerplan that was implemented. Dr. Buddy Newton, Medical Director of Antimicrobial Stewardship, laid the foundation for the plan based upon his vast experience and knowledge of the revisions to the SSC guidelines. This foundation was expanded upon and turned into an all inclusive multiple step plan of action by the committee consisting of Dr. David Ratcliff – Chief Medical Officer of the hospital, Dr. Kyle Hardy – Medical Director of ICU, Terri Church – nurse informaticist, Rebecca Cowie – critical care CNS, Sheryl Davis – Critical Care Director and CNS, and Teri Hayden – ED director (personal communication, 2013).

Specific Aims

The purpose of this prospective pre and post design study was to corroborate the effectiveness of EGDT care bundles as the standard of treatment in an urban hospital by evaluating the care of patients presenting to the ED with septic shock and to gather further data relating to collaboration between the ED and ICU in EGDT care bundles dealing with septic patients. Primary variables of interest included time to: fluid administration, vasopressor

administration, catheter insertion, initial antibiotics, and transfer to ICU - along with mortality rates and length of hospital stay. These data combined with that relating to compliance help to answer the question: Can sepsis EGDT be implemented in an urban hospital, with no prior experience in using a treatment protocol for septic patients, to benefit those patients? The primary focus of this research, then, is to determine if there is a difference between the pre and post implementation populations in the key variables of interest.

Methods

Approval was received from the hospital's quality improvement board and the University of Arkansas's institutional review boards (IRB) before the commencement of this study.

Sample

This study used non-random selection to divide its subjects into two groups: that of pre-implementation and that of post implementation. The post-implementation sample for this study consisted of all patients admitted to the ED between May 2013 and October 2013 with an admitting diagnosis of sepsis/septic shock and who were administered the Sepsis Powerplan care bundle. Information was compared to corresponding patient data for the same 6 month frame of the preceding year (2012) prior to implementation of the full care bundle as the pre-implementation group. In the context of this study, a diagnosis of sepsis in a patient was established with the presence of two or more of the following SIRS indicators:

- Temperature <96.8 F or >100.4 F
- Respiratory Rate >20
- Heart rate >90
- White Blood Count <4000 or >12000 OR >10% bands

- Systolic blood pressure <90, Glucose >150 in absence of Diabetes Mellitus

- Urine output < 35 cc/ hr (non hemodialysis patient)

- Altered mental status (acute), O2 saturation <92% on room air, or Lactate ≥4.0]

- A known or suspected infection (determined by treating physician)

For the purpose of this study, sepsis organ dysfunction was determined on a case by case basis by the physician in charge of the case based upon data obtained through lab tests as indicated by the Sepsis Powerplan.

Design

This study was constructed as a retrospective review prior to the implementation of the Sepsis Powerplan and a prospective review post implementation. Data from the 6 month period of patients with sepsis in 2012 served as the control and the data from the corresponding 6 months in 2013 served as the test group.

Variables

This study analyzed the following among both control and test groups:

- Time from admission to first fluid administration in minutes

- Time from admission to first vasopressor administration in minutes

- Time from admission to central venous arterial pressure (CVAP) catheter insertion in minutes

- Time from admission to initial antibiotics administration in minutes

    - Specific antibiotic administered

    - Whether a culture and sensitivity was drawn before antibiotic administered

- Time from admission to transfer to ICU (if necessary) in minutes

- Mortality Rates

- Length of hospital stay in days

- Compliance with bundle among providers as measured through documentation of all

    portions of Sepsis Powerplan administered

Procedure

The Sepsis Powerplan was administered to all patients presenting to the ED at the study

hospital who met the definition of sepsis. For these patients, admission to the ICU was

considered at the discretion of the physician in charge. Patients with severe sepsis, consisting of

the presence of two SIRS indicators plus one or more indicators of 'sepsis-related' organ

dysfunction were admitted to the ICU. All patients in septic shock –presenting with the two

sepsis indicators and hypotension unresponsive to appropriate fluid resuscitation were admitted

to the ICU. All patients were administered the care bundle and all data in the variables listed

came from the study hospital's medical records.

Data Analysis

To ensure the privacy of patients and staff, all data was de-identified according to HIPPA

guidelines for research. Each patient record was assigned a four digit alphanumeric code. The

first digit was either an S, indicating the patient is in the pre-implementation population, or an I,

indicating the patient is in the post implementation population, while the second digit will

indicate which floor [1-5] the patient was on in the hospital. The final two digits were a unique,

randomized two digit patient identifier number [00 – 99]. Data was collected for a 6 month span

from May 2013 – October 2013 for the post implementation. Corresponding data from the same

6 month frame of the preceding (2012) year were examined as the pre implementation data.

Results

The control group inclusionary criteria netted 39 patients, while the test group yielded 31 patients. Results were analyzed in a between-groups design, using two tailed t tests, z tests of proportions, and a Kruskal-Wallis one way ANOVA – all with an alpha level of 0.05 and the null hypothesis in all cases being that there was no difference between the test group and the control group. Two tailed t tests of time to fluid administration, $t = 1.504$, $p = 0.137$ with $df = 68$; time to vasopressor administration, $t = 0.355$, $p = 0.729$ with $df = 11$; time to antibiotic administration, $t = 1.476$, $p = 0.145$ with $df = 68$; time to ICU transfer, $t = 0.555$, $p = 0.587$ with $df = 16$; and length of hospital stay, $t = 0.545$, $p = 0.587$ with $df = 68$; failed to reveal a significant difference in the means between groups. Figures 1 and 2 show the similarity in means for these variables. A t test on time to central venous/arterial pressure (CVAP) catheter insertion was impossible due to insufficient data. Z tests of proportions on antibiotic culture and sensitivity obtainment, $z = -1.836$, $p = 0.0658$; and on mortality, $z = 1.836$, $p = 0.0658$ failed to reveal a significant effect. Figure 3 graphs the proportions for these variables. A Kruskal-Wallis one way ANOVA for categorical data revealed a significant effect for group on mortality, chi-squared $= 114.24$, $p = 0.0000$ with $df = 1$, indicating that variance in mortality can be accounted for by variance in the group. Therefore, according to t test results and z test results, the null hypothesis fails to be rejected while, according to the modified one way ANOVA, the null hypothesis is rejected.
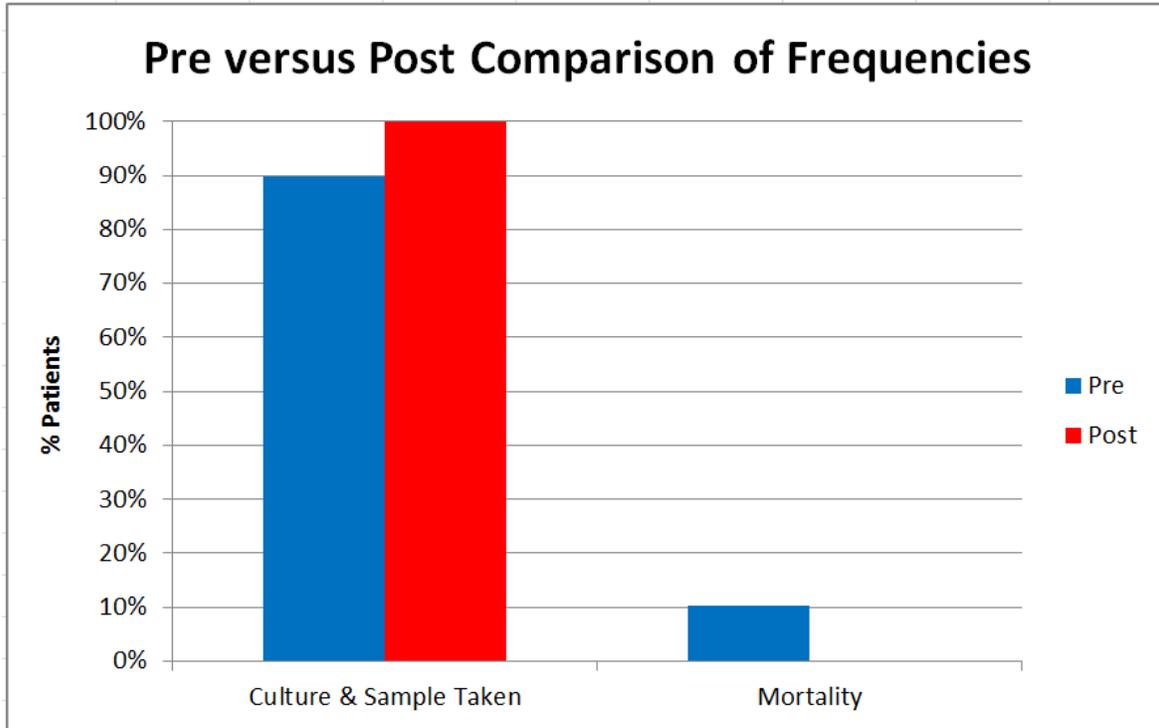
Figure 1.

Pre versus Post Comparison of "Length of Hospital Stay" Means
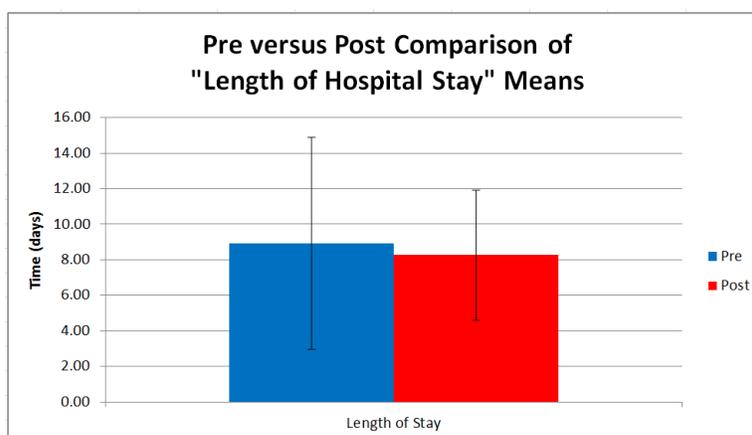
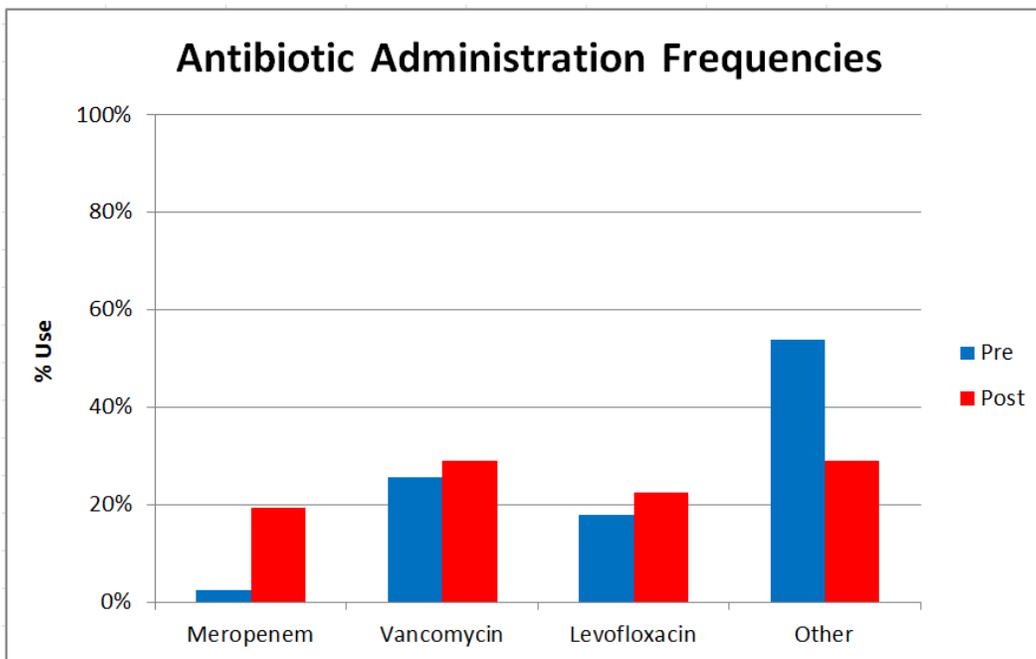- 1 - Pre versus post comparison of "Length of Hospital Stay" means

Figure 2
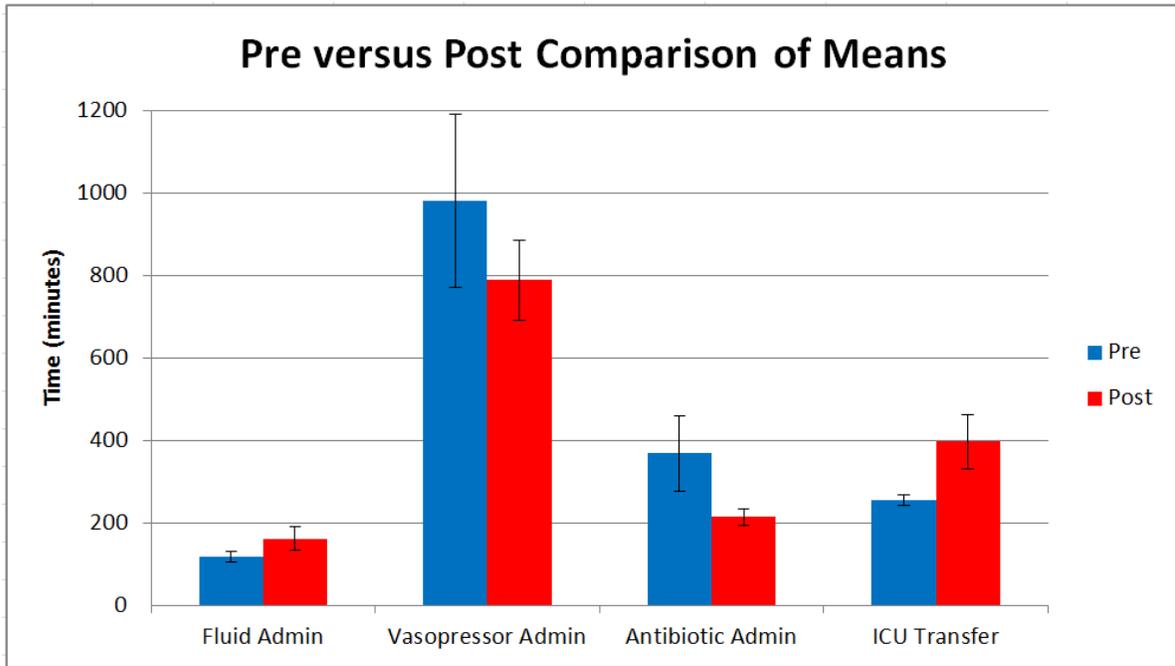
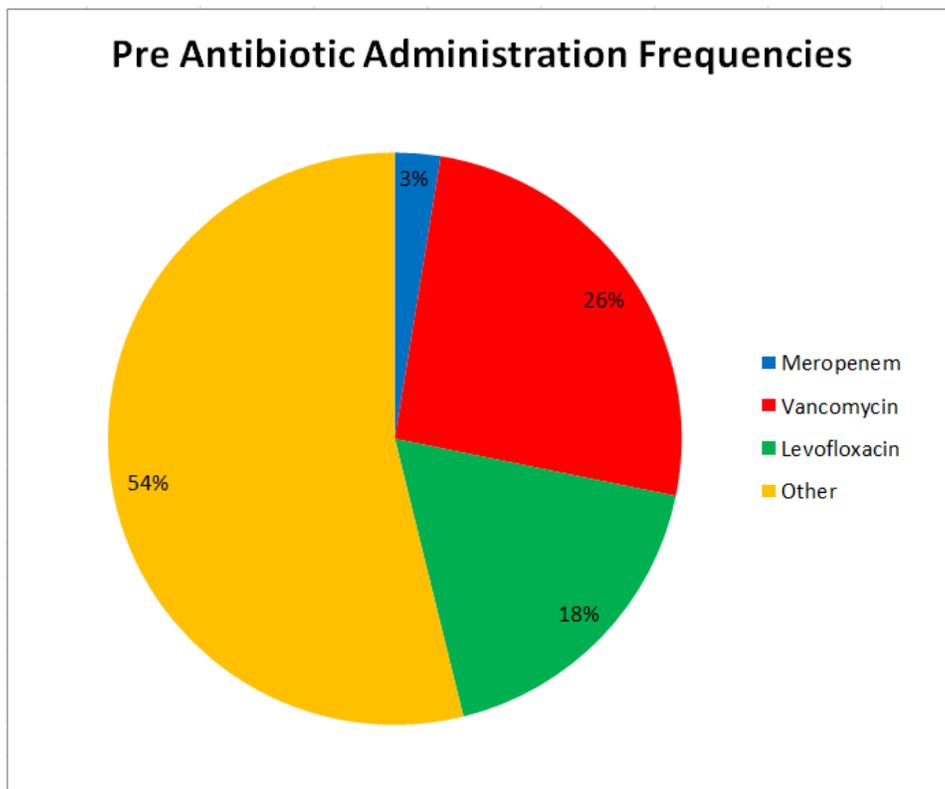**- 3 - Pre versus post comparison of means**

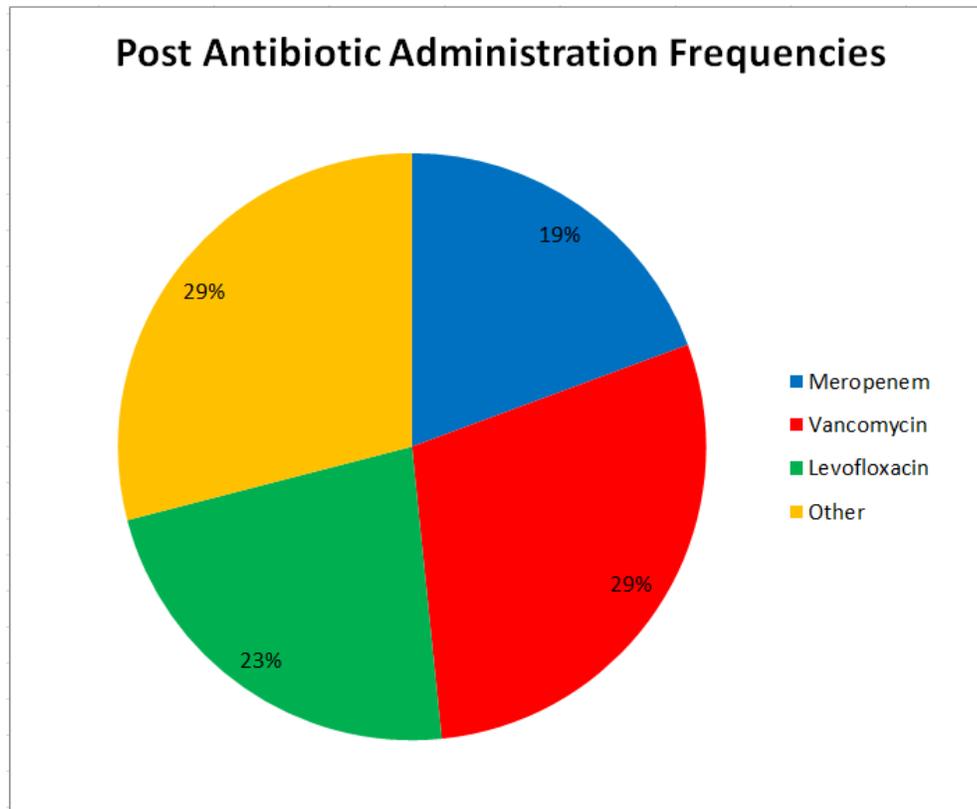Figure 3

- 4 – Pre versus post comparison of frequencies

Figure 4

- 5 - Antibiotic administration frequencies

Figure 5

- 6 - Pre antibiotic administration frequencies

Figure 6

Limitations

This study's primary limitation is that of time. Since the inclusion criteria is anyone

presenting to the ED at the facility of interest with SIRS indicators indicating a diagnosis of

sepsis over certain time frames for both pre and post implementation groups, a longer time of

study is necessary to have a larger sample size. A larger sample size would better reflect the

distribution of key variables amongst both pre and post populations, potentially yielding more

statistically relevant information. Another crucial limitation is that the design of the study was

created using an early draft of the implemented treatment protocol. Thus, data over some

variables of interest to the protocol was not collected while certain data over variables that were

actually collected was done so in a limited fashion, for example being categorical as opposed to

comparatively numerical. This results in a narrowing in the scope of this study as less relevant

information can be presented. The final limitation of the study is that a clear start time of patient

care was hard to identify given the provided documentation. In order to quantify how long it took for a given patient to receive fluid or antibiotics, not only is the time of administration required, so too is a clear time zero. This was not the case, however, as identifying exactly when a patient presented to the health system proved difficult as this factor was not defined in ED documentation and because mode of arrival to the ED varied between ambulance, where sometimes treatment would begin en route, and self transport, where treatment would not begin until after triage in the ED.

Discussion

Data was collected on all patients who presented to the facility of interest's ED meeting SIRS criteria for an initial diagnosis of sepsis. The pre-implementation group consisted of 39 patients who came into the ED between May and October of 2012 while the post-implementation group was made up of 31 patients who presented during the same months in 2013. Ultimately, the statistical analysis of data reveals that the only statistically significant difference between the pre-implementation and post-implementation groups occurs in regards to mortality. This in itself may demonstrate that the protocol had a significant impact on patient outcome. Yet, there is more to the data than just the final values of the statistical tests.

Comparison of Means

Figures 1 and 2 provide a clear illustration of the means of several variables of interest. With the first variable, time to fluid administration, it is interesting to see that, despite being statistically insignificant, the mean actually increased in the post-implementation group. There is, however, an outlier in the post-implementation group where fluids were not administered until much later in treatment (14.7 hours), when the patient was already on the floor. Since the sample sizes of both the control and test group are so small, it is worth analyzing the data sets with the

removal of the outlier to see if there was actually an effect on fluid administration time by the sepsis treatment protocol. Doing so lowers the mean in the test group to 137.93 and a t test comparing those means and the modified data sets yields t = .983 and p = .329, so the change is still statistically insignificant. Further study is required to identify what factors would potentially cause fluid administration time to increase in the test group.

In the second variable of interest, time to vasopressor administration, the mean time dropped from 981 minutes in the control group to 788 in the test group. But, the sample size for this variable is even smaller then the overall sample size for both groups because only those who clinically required vasopressors had them administered. This consisted of 6 patients in the control group and 7 in the test group. Because these numbers are so small, there is an extremely high degree of standard error in the means and it is no surprise that the difference in them is not statistically significant.

The next variable of interest, time to antibiotic administration, has a much lower, though statistically insignificant, average in the post-implementation group at 214 minutes than in the pre-implementation group at 368 minutes. As with fluid administration time, there was an outlier in the post-implementation data set where for an unknown reason antibiotic administration was delayed. Removal of this outlier lowers the post-implementation average further to 194 minutes. A t test on the modified data set yields t = 1.663 and p = .101 which is still statistically insignificant with an alpha level of 0.05. Though it is statistically insignificant it is a good indicator for the hospital that mean antibiotic administration time dropped so much between groups. It represents a step in the right direction and further analysis may reveal factors that lead to decreased antibiotic administration time that can be applied to fluid administration in order to decrease that time in the future. It is worth noting here that the updated SSC standards propose

rapid antibiotic administration and hemodynamic support with EGDT be accomplished within the first three hours of treatment (Dellinger et al., 2013). The hospital of interest falls within that guideline on fluid administration, but falls just shy of this standard for antibiotic administration. Further study into how other facilities decrease overall time to antibiotic administration is necessary to identify such practices and implement them in the facility of interest to further reduce antibiotic administration time.

With the next variable, time to ICU transfer, the average in the post-implementation group is about 20 minutes higher at 276 minutes than that of the pre-implementation group at 255 minutes. This difference was shown to be statistically insignificant and with approximately no difference in the standard error of the means it is safe to say that there is no meaningful difference between the two groups in that regard. It is interesting to note that the implemented Sepsis Powerplan is divided into two phases, mirroring the 2012 SSC guidelines of initially providing fluid resuscitation and antibiotics before moving on to more complex treatments like vasopressors and other hemodynamic therapies. The SSC's goals are to have the first phase of treatment be completed within three hours and the second to occur within six hours (Dellinger et al., 2013), while the facility of interest's goal is to do phase one in the ED and complete phase two in the ICU. In order to accomplish that goal then, further research must be done to identify and implement ways to decrease time in ED as the current time of approximately five hours to ICU is simply too long for the treatment protocols.

The final variable with means to compare is the length of hospital stay in days. The mean for the control group was 8.92 while the test group was 8.26. As this difference is statistically insignificant and the standard error of the means is approximately equal, it is safe to say that EGDT had no effect on the length of stay in this hospital. However, according to a CDC study in

2008 (Hall, Williams, DeFrances, & Golosinskiy, 2011), the average length of stay for those hospitalized for sepsis is 8.4 days. By this marker, the study hospital is just under the national average.

Comparison of Proportions and Frequencies

Figure 3 clearly shows that there is a difference between both groups when it comes to blood culture and sensitivity obtainment and mortality. In the pre-implementation group, 10% of patients did not have their blood cultures drawn before antibiotic administration while in the post implementation group, 0% of patients did not have their blood cultures drawn prior to antibiotic administration. At the same time, 10% of patients died in the pre-implementation group while 0% died in the post-implementation group. With a significance level of 95%, these results prove statistically insignificant since z tests result in a p value of .0658 for both. Yet, having no deaths in the post-implementation group is definitely noteworthy. If the significance level is dropped to just below 93.42%, these values are meaningful and the null hypothesis would be rejected. Therefore, accepting a 93% confidence level (as opposed to 95%) would have concluded that the difference in proportions for blood culture obtainment and mortality between groups did not occur by chance. This alone can't lead to the conclusion that the EGDT protocol directly caused these things to happen, but it is reasonable to presume that the protocol plus staff awareness and all other environmental factors post-implementation are leading to conditions in which blood cultures are taken more frequently and patients are dying less frequently. Further study is of course needed to verify this.

In conducting this study, data was collected not only on when antibiotics were administered but which antibiotics were administered first. Figure 4 shows the percentages with which different types of antibiotics were given and Figures 5 and 6 show these values as

percentages of the whole. The treatment protocol calls for a shotgun approach initially, that is using multiple broad spectrum antibiotics while blood cultures are running, before switching to more specific drug. According to the protocol, patients should receive the following antibiotics sequentially before switching to something more bacteria specific: meropenem, vancomycin, and levofloxacin. Unsurprisingly, most patients in the control group received a variety of antibiotics other than those three. Of interest is the proportion that actually received meropenem first in the test group. As can be seen in Figure 4 that is only about 19%, which is curious considering that it should be 100%. Further analysis as to why this occurred is necessary. Further education over the protocol may be necessary for those using it.

Analysis of Variance

Because 0% of patients in the post-implementation group died, while 10.2% of patients died in the pre-implementation group, a Kruskal-Wallis one-way ANOVA for categorical information was conducted to see if the variation in the group truly accounts for the variation in mortality. This test gets to the heart of this study as it attempts to say whether being in the pre or post group had an effect on whether or not a patient died. Since the p-value of this test is so low that it is essentially zero, the null hypothesis of equal variance per group was rejected at an alpha level of .0001. Because of this, it can be said with confidence that the variance in the group accounts for the variance in the mortality. As variance in group can only be pre and post and the variance in mortality can only be yes or no, then it can be said in this study with certainty that which group a patient was in does help to explain whether or not they died. While other factors could account for this and further analysis is necessary to say for sure due to the small number of subjects, this is a strong indication that EGDT at this hospital has indeed been effective at reducing mortality.

Recommendations

The scope of this study is limited to the hospital in which it took place, so recommendations based on this study's analysis will be aimed at this target hospital. Since the major weakness of this study is that the sample sizes are too low, in order for the hospital to determine whether or not its treatment protocol is having an effect on patient outcomes is to have continual monitoring with review. This will ultimately determine whether or not the trends seen by this study continue because eventually, the sample size of the post-implementation patients will become large enough to determine statistically significant differences on variables of interest. It is also recommended that the hospital continue to frequently educate its healthcare professionals on the treatment protocols. This is a new protocol implemented earlier this year, and given the low percentage of patients who received the appropriate first antibiotic in the test group, it is assumed that those using the protocol may not be familiar with it. Other more specific recommendations include: individual chart review for outlier patients to determine why indeed those patients were outliers, identifying systemically factors that would cause fluid administration time to increase with protocol implementation, and identification and implementation of methods to reduce overall antibiotic administration times and time spent in the ED before ICU transfer.

The Sepsis Powerplan is an important protocol which may prove to increase the identification and treatment of patients experiencing septicemia. It may have a major impact on overall mortality rates in these high risk patients. Implementation of such a protocol needs continuous evaluation for compliance with implementation guidelines to maximize its impact on patient care.

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