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ANALYSIS OF THE EFFECTIVENESS FOR DEATH PREVENTION OF PATIENTS INCLUDED IN A SEPSIS PROTOCOL

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Abstract: Sepsis is a systemic pro-inflammatory response caused by bacterial, fungal, viral, autoimmune diseases causing dysfunction of one or more organs or systems. In this context, the aim of this study was to compile the literature on the impact of implementing the sepsis protocol on lower mortality and morbidity, to elucidate risk factors and possible interventions. A total of 55 studies were identified according to our search strategy. After applying the adopted inclusion and exclusion criteria, a total of 31 studies in Medline/Pubmed and Medline/BVS were excluded. Then the titles, abstracts and the full text were read, 20 of the 24 references were excluded based on the eligibility criteria. Thus, 4 references were selected for full text evaluation. Finally, four articles were eligible for qualitative evaluation. Despite the early institution of therapeutic measures advocated in the international literature, mortality from sepsis in the institution in question is still high. All references demonstrate the association of better prognosis for early diagnosis of sepsis with respect to protocol adoption, with P-value lower than the significance level = 0.05. This review corroborates that there are still gaps in the treatment of sepsis. However, the implementation of this protocol allows for a better diagnosis of sepsis, reduces possible early sepsis diagnoses, and promotes the effective use of antimicrobial agents in this population. Therefore, we need to investigate more closely the associated risk factors and the implementation of sepsis protocols to obtain a possible effective intervention.
Keywords: Sepsis; Infection; Mortality; Protocol.

INTRODUCTION

The first description of sepsis was found in Egypt, in a papyrus from 1600 BC; the etymology of the word comes from the ancient Greek term sechas which means "putrefaction"

or the "decay of organic matter". The earliest use of the Greek term is found in Homer's book Iliads and the Hippocratic corpus in the 4th century BC. More than 2,000 years passed before, again, a new definition of the etiology and a new discussion of approaches were made. Sepsis is a systemic pro-inflammatory response caused by bacterial, fungal, viral, autoimmune diseases causing dysfunction of one or more organs or systems. It is a syndrome that carries a high mortality rate, leaving serious sequelae when it survives. (FLEISCHMANN et al., 2016; MARKWART et al., 2014; SALES JÚNIOR et al., 2006).

However, it is one of the main causes of in-hospital death and in urgencies and emergencies (SALOMÃO et al., 2011). Despite the advancement of medicine and the use of modern antibiotics and new resuscitation protocols, the response is still low, as Sepsis involves several extremely complex chains of events, pro-inflammatory and anti-inflammatory processes, humoral and cellular reactions and abnormalities circulatory disorders, the diagnosis is extremely difficult and complex due to the nature of the variables and the non-specificity of the signs and symptoms (ARANGO-GRANADOS et al., 2010; CARVALHO, 2021; WESTPHAL, 2011).

Thus, it is responsible for 25% of occupation of beds in therapy units in Brazil, tensive. It is currently the leading cause of death in ICUs and one of the leading causes of late hospital mortality, surpassing myocardial infarction and cancer (Harpaz, 2013). Data from Brazilian epidemiological studies, coordinated by the Instituto Latino Americano de Sepse (ILAS 2015), indicate that the mortality rate in our country can reach 55% of patients with sepsis in Brazilian ICUs. In the last decade, the incidence rate of the disease increased between 8% and 13% compared to the previous decade, accounting for more deaths than some types of cancer, such as breast and bowel cancer (WHO 2016).

Recently, research on infection related to health care of the general population has been at the heart. However, this review aims to highlight this process, as it subsidizes the development of more effective actions and treatments aimed at communities. In this context, the aim of this study was to compile the literature on the impact of implementing the sepsis protocol on lower mortality and morbidity, to elucidate risk factors and possible interventions.

METHODOLOGY

This is an integrative review study that was designed based on the criteria established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide, considering the flow diagram and the PRISMA checklist. Thus, from the guiding question: "Analysis of the effectiveness for preventing deaths of patients included in a sepsis protocol?" the articles were searched.

Keywords were defined according to the PICOS model as follows:

1. Population: patient with sepsis;
2. Intervention: protocol implementation;
3. Comparative: control (absence of protocol);
4. Results (variables): clinical improvement and reduction of mortality and morbidity;
5. Study design: observational studies

SEARCH IN THE LITERATURE

The survey of articles was carried out in the following databases: Medline/BVS and Medline/Pubmed. The following descriptors and their combinations in Portuguese and English were used to search for articles: "Sepsis AND Antibioticoterapia AND Mortalidade // Sepsis AND Antibiotic therapy AND mortality".

INCLUSION AND EXCLUSION CRITERIA

The selection of articles was guided by inclusion and exclusion criteria. The inclusion criteria defined for the selection of articles were: articles published in Portuguese, English; original articles in full that portray the theme related to the review and articles published and indexed in the aforementioned databases in the last 15 years.

The exclusion criteria defined for the selection of articles were non-original articles, dissertations and theses, articles that addressed the subject, but from a different point of view.

After applying the inclusion and exclusion criteria, the articles were identified. The screening of studies was carried out by reading and analyzing the titles and abstracts of all articles identified in each database, guided by the adopted inclusion and exclusion criteria. In the eligibility phase, after defining the articles to be included in each database, duplicate articles were excluded.

RESULTS

SELECTION OF STUDIES

A total of 55 studies were identified according to our search strategy. Among them, no duplicate article was presented. After applying the adopted inclusion and exclusion criteria, a total of 31 studies in Medline/Pubmed and Medline/BVS were excluded. Then the titles, abstracts and the full text were read, 20 of the 24 references were excluded based on the eligibility criteria. Thus, 4 references were selected for full text evaluation. Finally, four articles were eligible for qualitative evaluation. The selection process for identifying eligible studies is included in the review, shown in Figure 1.

CHARACTERISTICS OF THE INCLUDED STUDIES AND ANALYSIS OF THE EFFECTIVENESS OF PREVENTING DEATHS OF PATIENTS INCLUDED IN A SEPSIS PROTOCOL

The main characteristics of the included studies are presented in Chart 1. In the study by Verena Ribeiro in 2011, the sample of N = 144 septic patients, the mean gender and age group respectively: 65 women (44.8%) and 79 men (55.2%) approximately, with a mean age ± standard deviation (SD) of 73.1 ± 14.6 years. Regarding, mortality in septic patients in the ICU (Intensive Care Unit), as well as hospital mortality, is higher than in non-septic patients, demonstrating the impact of this clinical syndrome and emphasizing the importance of early treatment to minimize the impact on clinical outcomes. It was also found that the in-hospital mortality rate of patients with sepsis (60.0%) was much higher than that of ICU patients (38.5%). This fact may support a more cautious approach to these patients, including at ICU discharge, as one study suggests that patients with pre-existing sepsis may be at risk of its complications.

Regarding the reference by Maria Cristina F. Guedes Pinto from 2013, the sample of N = 144 newborn patients, the mean gender: 68 women (50%) and 68 men (50%). Regarding the implementation of the ANVISA manual as a protocol to improve the diagnosis of neonatal sepsis, there was a decrease in the diagnosis of suspected early sepsis and, therefore, a decrease in the use of antimicrobials, especially the first regimen (ampicillin + gentamicin). Probably earlier, fewer diagnoses of sepsis and therefore less need for care for these newborns with suspected sepsis were the most important results of this study.

According to Larissa Estela Ferreira Jacó de Menezes from 2018, the sample of N = 412 patients (55.3 years old), 58%

of whom were male. Among the patients, 80.1% were included in the protocol within the recommended time, 79.9% had a lactate collection and 91.7% a blood culture on time. Thus, the study corroborates that patients included in the protocol had a significant difference when comparing the 3 years for both variables (p<0.05). The same can be seen in the comparison between the years 2013 and 2014, and 2013 and 2015, for both parameters. Finally, 87.4% of patients started antibiotic therapy within the recommended period for the analyzed period.

According to Karen Zelinda de Bortoli Bonatto of 2022, the sample of N = 67 remaining patients, most of them were female, 35 (52.2%), with a mean age of 67.0 ± 19.4 years. Thus, the predominant infectious focus on admission was the lung, predominating infections by Gram-negative bacteria, and most patients received resuscitation with crystalloid, in addition to broad-spectrum antibiotic therapy. Despite the early institution of therapeutic measures advocated in the international literature, mortality from sepsis in the institution in question is still high.

The results showed that in the studies selected from the inclusion and exclusion criteria. all references [1-4], demonstrates the association of better prognosis for early diagnosis of sepsis with respect to protocol adoption, with P-value less than significance level = 0.05.
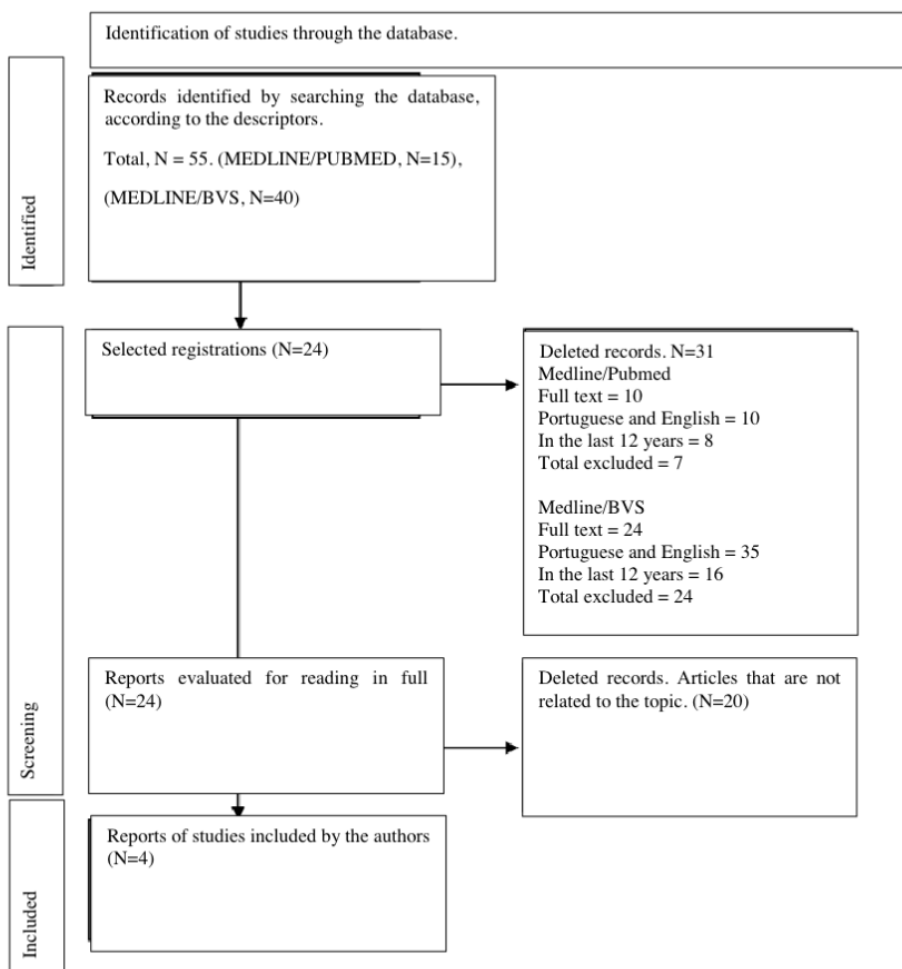

Figure 1: Flowchart for selection process, identification, screening, eligibility and included.

Number	Title/Author	Publication year	Study design	Goals	Methodology	Main results
1	Clinical impact of sepsis diagnosis upon admission to the ICU of a private hospital in Salvador (Bahia/Juncal)	2011	Tracking studies	To describe the clinical characteristics, laboratory data and clinical outcome of septic and non-septic patients admitted to the ICU of a private hospital in the city of Salvador (Bahia) and to identify clinical variables related to the worst prognosis of septic patients.	A longitudinal study was carried out including all patients admitted to the general ICU of the Hospital Português, Salvador (Bahia), between June 2008 and March 2009. On admission to the ICU, 2 groups of patients were identified as septic and non-septic. Epidemiological, clinical, and laboratory data were collected, and the acute physiology and chronic health Evaluation II (APACHE II) score was calculated.	Of the 144 patients in the study, 29 (20.1 percent) were septic. Among septic patients, 55.2% were male, mean age was 73.1 ± 14.6 years, and mean APACHE II score was 23.8 ± 9.1. In the non-septic group, 36.3% were male, mean age was 68.7 ± 17.7 years, and mean APACHE II score was 18.4 ± 9.5.
2	Implementation of a protocol proposed by the National Health Surveillance Agency for the use of antibiotics in very low birth weight newborns.	2013	Prospective study	To analyze the implementation of a protocol proposed by the National Surveillance Agency (ANVISA) to improve the diagnosis of sepsis in very low birth weight newborns....	This was a prospective study that evaluated the implementation of a protocol involving clinical and laboratory criteria (Rodwell's hematological scoring system and serial measurements of C-reactive protein), recommended by ANVISA, to improve the diagnosis of neonatal sepsis in newborns of very high Low weight.	316 very low birth weight newborns participated in the study. There was no difference between the groups regarding general clinical characteristics in the periods studied. There was, however, a decrease in the number of diagnoses of probable early sepsis ($p<0.001$), use of antimicrobial regimens ($p<0.001$) and infection-related mortality ($p=0.009$, and $p=0.049$, respectively)
3	Epidemiological profile and analysis of effectiveness for preventing deaths of patients included in a sepsis protocol	2019	Observational study	To evaluate cases of sepsis and septic shock, checking the epidemiological profile, treatment, adherence to international recommendations and degree of effectiveness of interventions, to analyze their effectiveness in reducing mortality.	This is a cross-sectional observational study with a review of sepsis and septic shock consultations between April 2013 and December 2015. As for the effectiveness in preventing deaths, the period was from 2014 to 2015.	A total of 412 patients (55.3 years old) were included, 58% of whom were male. Among the patients, 80.1% were included in the protocol within the recommended time, 79.9 had a lactate collection and 91.7% had a blood culture on time ($p<0.05$). They started antibiotic therapy within 87.4 of the sample.
4	Management of septic patients admitted to Hospital Universitario Santa Terezinha	2022	Risk factors	To analyze the management of septic patients admitted to the emergency room of a university hospital in the Midwest region of Santa Catarina.	Documentary, retrospective, descriptive and quantitative study, carried out in the medical records sector of the Hospital Universitario Santa Terezinha, with data collected from the 67 medical records of patients treated between February and June 2018.	Predominance of women, age 67.0 ± 19.4 years; prevalent infectious focus on pulmonary admission, predominance of gram-negative infection; volume resuscitation predominantly with crystalloid, prevalence of broad-spectrum antibiotic therapy, 29.9 per center were admitted to the ICU.

Table 1: Description of the articles selected with the variables: Title of study/Author, year of publication, objectives, methodology and main results.

CONCLUSION

This review corroborates that there are still gaps in the treatment of sepsis. However, the implementation of this protocol allows for a better diagnosis of sepsis, reduces possible early sepsis diagnoses, and promotes the effective use of antimicrobial agents in this population. Therefore, we need to investigate more closely the associated risk factors and the implementation of sepsis protocols to obtain a possible effective intervention.

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