

Effectiveness of continuous veno-venous haemofiltration in patients with septic shock

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No subsidies have been received for this study.

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KEY WORDS: continuous veno-venous haemofiltration, septic shock, critical, filter, effectiveness.

ABSTRACT

Introduction. Renal Replacement Therapy such as Continuous Veno-Venous Haemofiltration (CVVH) in patients with septic shock as this disease shows a very high morbidity and mortality rate in hospital ICUs. Data to help determine the effectiveness of CVVH in patients with septic shock will be discussed and analysed.

The aim of this research is to evaluate the effectiveness of continuous veno-venous haemofiltration in patients with septic shock by means of a systematised review.

Material and methods: For this study, a systematised review structured according to the PRISMA® system was carried out. After formulating the research question using the PICO® system, a search was carried out in different databases with the search terms "Continuous renal replacement therapy AND shock septic". Articles in both Spanish and English were selected, especially those published in the last 5 years. Articles with low scientific evidence were not selected.

Results: Twelve scientific articles were selected in accordance with election criteria for critical reading with the CASPe system. Each of the articles was classified according to author, year of publication, level of prevalence, socio-demographic data and level of SIGN evidence. The main biases that occurred were selection and publication biases.

Conclusions: Continuous Venous-Venous Haemofiltration in patients with septic shock is highly effective, although despite its practice in patients with cardiac disease it does not show any major benefits.

INTRODUCTION

In recent years nursing has undergone a change in activities and competences have increased in the hospital and outpatient setting. Nurses now perform highly significant procedures for the haemodynamic stabilisation of patients, in this case in the Intensive Care Unit (ICU). These advances are joined by technology for the benefit of critical patients, such as Continuous Renal Replacement Therapy (CRRT). These techniques are implemented using specialised equipment including blood pumps, blood collection and return circuits, membrane filters and monitors to control blood flow and treatment parameters. The main methods used in CRRT include Continuous Veno-Venous Haemofiltration (CVVH), Continuous Venous Haemodialysis (CVHD), and Continuous Venous Haemodiafiltration (CVHDF). This research focuses on one of the CRRTs – haemofiltration in patients with septic shock as this disease shows a very high morbidity and mortality rate in the Intensive Care Unit (ICU) in hospitals. Data that helps determine the effectiveness of CVVH in patients with septic shock will be discussed and analysed, and the results and conclusions will be presented.

MATERIAL AND METHODS

For this study, a systematised review structured according to the PRISMA® system was carried out. After formulating the research question with the PICO® system, articles in Spanish and English were selected, especially those published in the last 5 years. Articles with low scientific evidence were not selected. There was no conflict of interest and the work was carried out taking into account the bioethical principles of all research.

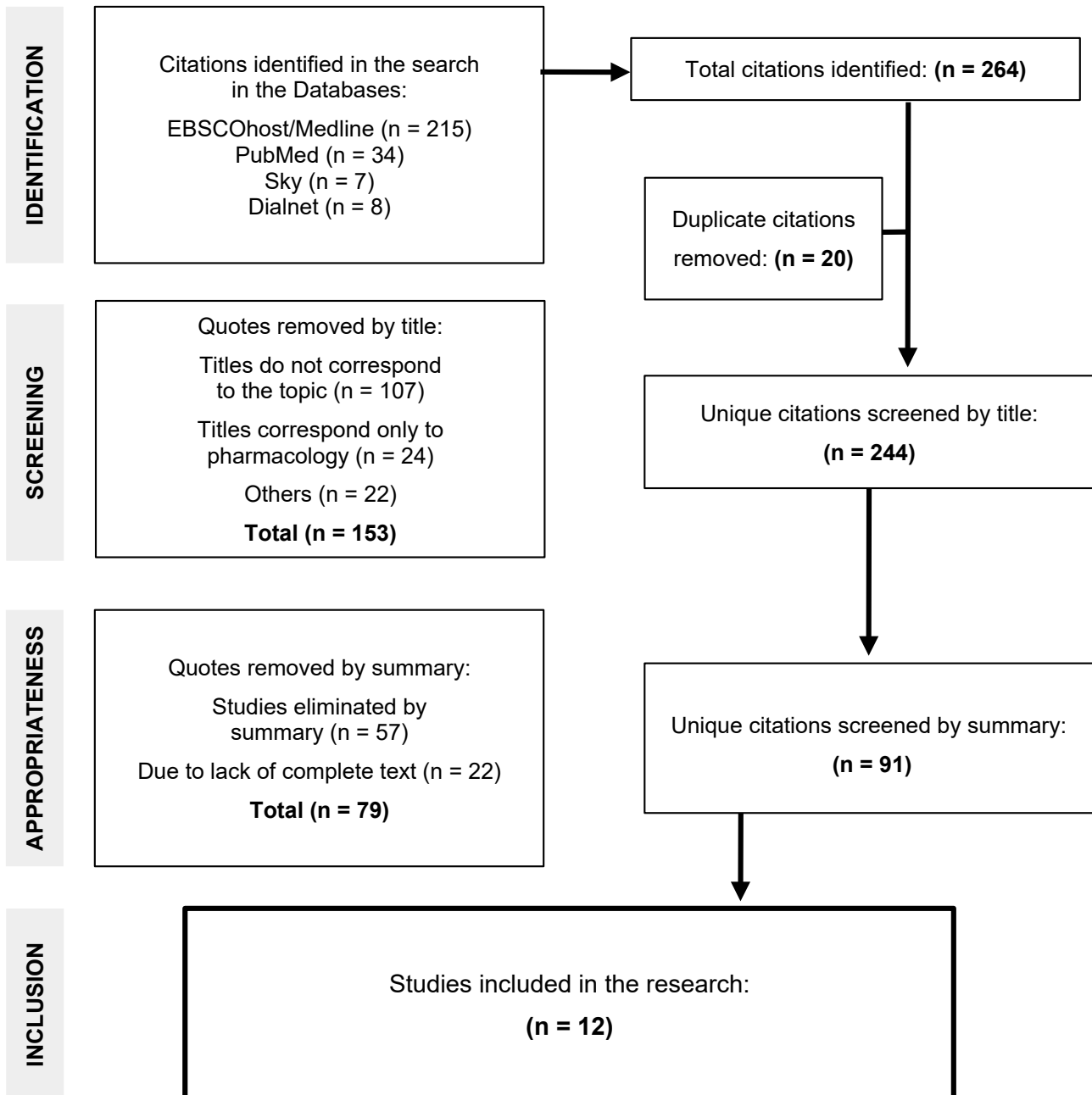
Research question (PICO)®: P: Adult intensive care patients diagnosed with septic shock I: Patients undergoing CVVH. C: No comparison made. O: Favourable results by decreasing the mortality rate in these patients.

At the beginning of the systematised search, a series of English descriptors were selected using the Medical Subject Headings (MeSH)(34), in addition to the Health Sciences Descriptors (DeCS)(34) on the BIREME portal. The descriptors selected were those shown and used in the search equation: Continuous Renal Replacement Therapy, Septic Shock Haemofiltration, Cardiovascular Failure, Septic Shock, Continuous Venous Effectiveness Haemodiafiltration

The search was carried out on the following scientific databases (DB), EBSCOhost MEDLINE, PUBMED, SCIELO and DIALNET. For the selection of the articles of interest, a series of search terms were formulated, the most relevant being “Continuous renal replacement therapy and septic shock”. From these, a total of 264 articles were obtained from which 12 scientific articles were finally chosen after an exhaustive reading as described in the databases used with the Boolean connectors (AND, OR, NOT).

RESULTS

After reading the articles selected, the research evidence was assessed in order to evaluate their methodological quality. The articles were therefore analysed according to the type of research, namely 2 case studies, 1 multicentre study, 9 observational cohort studies and clinical trials. They were analysed using the Scottish Intercollegiate Guidelines Network SIGN(35), while bias was measured using the CASPe(36) scale. The scales used, which can be found in the appendices of this paper, are the checklist (CASPe) and questionnaire (SIGN) scales from which a score was obtained for each article. The article selection process is reflected in the flow chart suggested by the PRISMA® guide.



Article selection process. (Source: Designed in-house)

Most research was conducted in Europe; 2 studies were conducted in France, 1 study in the Netherlands, 1 in Latvia, 1 in Germany, 1 in Poland, 1 in Rome, 1 in Spain, 1 in China, 1 in Korea, 1 in Baltimore USA, and 1 in Chile. Consequently, there is more research in Europe in relation to CVVH in septic shock patients.

With regard to the typologies of the studies selected, and after preparing the corresponding absolute frequency table, we can state that the majority were retrospective observational studies (37%), followed by prospective observational studies (18%). The least predominant studies in this research were case studies (18%), Multicentre studies (9%), and Randomised Clinical Trials (9%).

The SIGN® levels of evidence also differed according to the type of studies included in our Systematic Review (SR). Studies with a SIGN® 2+, which are well-conducted cohort or case-control studies with a low risk of confounding or bias and a moderate probability that the relationship is causal, predominate at 34%.

25% of the studies were SIGN® 2-, which corresponds to cohort or case-control studies with a high risk of confounding or bias and a significant risk that the relationship is not causal, followed by SIGN® (17%), 3 non-analytical “case studies” (8%), 1++ is a high quality meta-analysis, a randomised clinical trial with very low risk of bias, the same as SIGN® 1- an RCT with high risk of bias and finally SIGN® 2++ which corresponds to high quality cohort controls. In this case, it should be noted that 34% of the studies selected have a well-conducted level of evidence with a low risk of bias or confounding, with SIGN® ranging from 2- to 3.

Of the variables in this research study, 2 specific variables were broken down as part of the factors influencing the effectiveness of CVVH in patients with septic shock:

Age:

The patients who were treated with CVVH were analysed in this section using quantitative methodology. The mean age of the patients with septic shock in the literature consulted was 60.3, and a division was established according to age ranges.

Clinical Profile:

According to Franco Turania et al.(21), one of the authors of the study, 60% of patients with infections by gram + and - bacteria are affected, although patients with comorbidities such as cardiovascular diseases, according to Georgijs Moises et al.(26), 55.6%, are also affected. Mortality in patients with septic shock may vary depending on the factors mentioned above.

DISCUSSION

The study 'Assessment of patient safety in the clinical practice of renal replacement therapy in intensive care units' by Suarez et al. (45), assesses the importance of performing CRRT in critical patients; it has been scientifically proven that this therapy, when continuous, improves haemodynamic stability, reduces the infusion dose of vasoactive drugs such as noradrenaline, maintaining a MAP of 65 mmHg in the first instances, serum lactate levels decrease (taking into account that elevated serum lactate in patients with septic shock indicates a serious condition), decreasing tissue perfusion and cardiovascular dysfunction; according to studies high levels indicate an increase in mortality.

Analysing the aforementioned article by Suarez et al.(45) each patient with septic shock has individual characteristics and comorbidities that must be taken into account when deciding on heparinisation, including pre-existing conditions that increase the risk of bleeding, the presence of organ dysfunction or the need for other anticoagulant therapies. Although the articles selected do not address percentages on the effectiveness of CVVH in patients with septic shock, each of them has been thoroughly analysed, resulting in six of the 12 articles selected, namely those by Yining Li et al.(37), Zuccari et al. (40), Grzegorz Kade et al.(41), Bo Ra Yoon et al.(42) Franco Turania et al.(47), Gonzalo Ramirez et al. (46). These articles all show that CVVH is effective by demonstrating a significant reduction in inflammatory mediators such as pro-inflammatory cytokines like tumour necrosis factor alpha (TNF- α), interleukin 1 beta (IL1 β) and Interleukin 6 (IL-6), These cytokines are released mainly by the immune system such as macrophages and lymphocytes in response to infection. When CVVH is performed, it causes a decrease in these values in the body causing a modulation of the excessive inflammatory response seen in septic shock via the bloodstream, and tissue damage is reduced. In the case of endotoxins, as they are components of the cell wall of Gram- bacteria, the aforementioned authors in their research emphasise that by means of CVVH the elimination of high molecular weight substances by adsorption is significantly noted. Willem Pieter Brouwer et al.(48) and Georgijs Moises et al.(39), however, emphasise that for the elimination of endotoxins it is important to take into account that their effectiveness is associated with the appropriate filter according to the molecular weight of the endotoxins. In relation to the factors influencing the effectiveness of CVVH in patients with septic shock, the age of the patients was analysed and the mean age of the patients was 65, which was 75% of the patients who have undergone the therapy. In relation to the clinical record of the 5 authors Guangwei Yu et al.(38), Willem Pieter Brouwer et al., Samuele Zuccari et al.(40), Victor Schwindenhammer et al. (43) and Lanping Chu et al.(44), who mention abdominal sepsis as one of the most frequent causes of ICU admission, 3 of them focus on acute respiratory infection with emphasis on pneumosepsis as a trigger, stating that pathogenic microorganisms such as bacteria, viruses and fungi infect the lungs and thus generate an inflammatory response in the hospital stay before the patient is admitted to the Intensive Care Unit. Urinary tract infection is also mentioned by two authors – Manuel Zuccari et al.(40), Lanping Chu et al.(44) – who agree that the urinary tract is susceptible to colonisation and multiplication of bacteria and initially triggers a local inflammatory response. In the cases presented in the aforementioned studies they speak of bacteraemia caused by an uncontrolled systemic inflammatory response (sepsis). Patients who are affected by cardiac diseases are at higher risk of developing serious complications, as stated by Guangwei Yu et al.(38) in their specific study on CVVH in patients with left ventricular dysfunction (LVD). The author makes a comparison with patients presenting septic shock without pre-existing heart disease and patients with LVD, giving a high mortality rate in these patients. Guangwei Yu et al.(38) mentions that survival is very difficult and does not associate beneficial outcomes with treatment; the function of CVVH is compromised by hypotension since the left ventricle (LV) decreases cardiac output causing generalised hypotension. CVVH requires sufficient blood flow to extract and filter blood through the extracorporeal circuit. He also mentions renal damage as a consequence, so it is important to assess the haemodynamic and cardiac condition of a patient before initiating CVVH(38). Similarly, cholangitis as a clinical record is mentioned by Lanping Chu et al.(44)

when he notes that bacteria present in the bile ducts enter the bloodstream, carrying toxins and endotoxins; these pathogens trigger a systemic inflammatory response and is relevant in their study. It is important to bear in mind that patients who present septic shock before admission to the ICU have comorbidities that are risk factors for each patient, which may vary from patient to patient. Of the twelve articles selected for this study and placed in the flow diagram and selection of articles, cardiovascular diseases predominate, among them HBP, coronary heart disease and heart failure. Authors such as Suarez MT et al. say that liver failure directly affects the immune response, renal diseases such as CRI influences the response of the patient with septic shock and CRRT, and in the same way, patients with diabetes mellitus are mentioned by authors such as Guangwei Yu et al.(38), Willem Pieter Brouwer et al.(48) and Georgjis Moises et al.(39), who treat this disease as a chronic condition that stresses blood sugar control and increases the risk of complications. Patients with neoplasia are also mentioned; Georgjis Moises et al.(39) are of the opinion that these patients develop infections because their immune system is weakened by their oncological treatment.

Limitations of the study

One of the main biases in all scientific research is the methodological limitations that are inherent to the typology chosen, so it is necessary to be accurate and honest in each of the steps to follow.

Future lines of research

We would propose conducting a systematised study in continuity with CVVH on patients with higher plasma Glutathione Reductas (GR) activity, which has a fatal outcome in patients, before patients with lower GR.

CONCLUSIONS

It is evident that a large number of articles related to the research work were carried out in Europe. The evidence in the research shows that they are one of the pioneers in performing CRRT in patients diagnosed with septic shock. As of today this therapy is on the list of first choice (31).

In Spain scientific research is being carried out in the city of Barcelona; it focuses on the research on Intermittent Renal Replacement Therapy. The researchers say that the effectiveness is higher, they talk about patient safety and the most frequent clinical complications such as: arrhythmias, dyspnoea, pruritus, and above all allergic reaction to the filter. As for the technical complications they have experienced during the process, they mention the partial or total coagulation of the circuit, and so we would underline the blood extravasation or haematoma in the arteriovenous fistula and exit of the central venous catheter as the most important. The pertinent corrective action was taken during the process. 35% of patients with septic shock were admitted to hospital during the investigation. The importance of the use of the membrane in the haemofilter and the prevention of complications was analysed in this article, given that our research focuses on Continuous Veno-Venous Haemofiltration. The result was that critical patients effectively subjected to RRT overcame the phase of greatest haemodynamic instability in those indicating CRRT, although the therapy that is most commonly carried out in this area is Intermittent, which also gives positive results (45).

CVVH has been shown through research to be highly effective in patients with septic shock, although the scientific evidence does not support its efficacy in its entirety, and there is no absolute consensus on the therapy.

The severity of the **clinical record**. Research has shown that continuous veno-venous haemofiltration is highly effective in patients with septic shock.

Comorbidities. It is important to note that the patients most vulnerable to septic shock are those with comorbidities such as cardiovascular disease.

Age. From the research conducted, it would seem that the most vulnerable patients are the elderly, with a mean age of 65.

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