Med Clin (Barc). 2017;xxx(xx):xxx–xxx

MEDICINA CLINICA

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Original article

Risk factors for nosocomial infections in patients receiving extracorporeal membrane oxygenation supportive therapy☆

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ARTICLE INFO

Article history:
Received 12 September 2016
Accepted 23 March 2017
Available online xxx

Keywords:
Extracorporeal membrane oxygenation
Infection factors
Nosocomial infection
Drug susceptibility
Drug-resistance phenotype

ABSTRACT

Background and objective: The aim of this study was to analyze risk factors for nosocomial infection (NI) in patients receiving extracorporeal membrane oxygenation (ECMO) support.
Patients and methods: Clinical NI data were collected from patients who received ECMO support therapy, and analyzed retrospectively.
Results: Among 75 ECMO patients, 20 were found to have developed NI (infection rate 26.7%); a total of 58 pathogens were isolated, including 43 strains of gram-negative bacteria (74.1%) and 15 strains of gram-positive bacteria (25.9%). Multi-drug resistant strains were highly concentrated and were mainly shown to be *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and coagulase-negative staphylococci. Incidence of NI was related to the duration of ECMO support therapy and the total length of hospital stay, and the differences were statistically significant ($P < 0.05$). A prolonged period of ECMO support extended the hospital stay, but it did not increase the mortality rate. However, an elevated level of lactic acid increased the mortality rate in this study population.
Conclusions: ECMO-associated secondary NIs correlated significantly with the length of hospital stay and with the duration of ECMO support. Therefore, to reduce the incidence of ECMO-associated NIs, preventive strategies that aim to shorten the duration of ECMO support therapy and avoid lengthy hospitalization should be applied, wherever possible.

Factores de riesgo de las infecciones nosocomiales en pacientes que reciben oxigenación por membrana extracorpórea

Palabras clave:
Oxigenación por membrana extracorpórea
Factores de infección
Infección nosocomial
Susceptibilidad a fármacos
Fenotipo de resistencia a fármacos

RESUMEN

Antecedentes y objetivo: El objetivo de este estudio fue analizar los factores de riesgo de la infección nosocomial (IN) en pacientes que reciben soporte de *extracorporeal membrane oxygenation* (ECMO, «oxigenación por membrana extracorpórea»).
Pacientes y métodos: Se recolectaron los datos clínicos de las IN de los pacientes que recibieron tratamiento de soporte ECMO, analizándose retrospectivamente.
Resultados: Entre los 75 pacientes con ECMO, se encontró que 20 habían desarrollado IN (tasa de infección del 26,7%), aislándose un total de 58 patógenos, incluyendo 43 cepas de bacterias gramnegativas (74,1%) y 15 cepas de bacterias grampositivas (25,9%). Las cepas resistentes a múltiples fármacos se hallaban altamente concentradas, componiéndose principalmente de *Acinetobacter baumannii, Pseudomonas aeruginosa* y estafilococos coagulasa negativos. La incidencia de IN se relacionó con la duración del tratamiento de soporte ECMO y la estancia hospitalaria total, siendo las diferencias estadísticamente significativas

☆ Please cite this article as: Sun G, Li B, Lan H, Wang J, Lu L, Feng X, et al. Factores de riesgo de las infecciones nosocomiales en pacientes que reciben oxigenación por membrana extracorpórea. Med Clin (Barc). 2017. http://dx.doi.org/10.1016/j.medcli.2017.03.038

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(p < 0,05). Un período prolongado de soporte ECMO ampliaba la estancia hospitalaria, aunque no incrementaba la tasa de mortalidad. Sin embargo, la elevación del nivel de ácido láctico incrementaba la tasa de mortalidad en esta población de estudio.
Conclusiones: Las IN secundarias asociadas a ECMO guardaron una correlación considerable con la duración de la estancia hospitalaria y la duración del soporte ECMO. Por tanto, para reducir la incidencia de las IN asociadas a ECMO, deberán aplicarse estrategias en aras de reducir la duración del tratamiento de soporte ECMO y evitar la hospitalización prolongada, cuando ello sea posible.

Introduction

Extracorporeal membrane oxygenation (ECMO) support requires direct vascular intubation, in combination with various other invasive interventions specific to intensive care, increasing the risk of life-threatening complications, such as hematogenous infections. Identifying and reducing risk factors in ECMO-related nosocomial infections (NI) may improve patient survival rates. Several reports have previously highlighted the risk factors of ECMO-related NIs, in China and elsewhere.[1–9] Wong et al.[10] examined the NI rate in ECMO patients and identified the duration of ECMO support therapy as the main risk factor leading to complications. Another study reported on positive reports of blood culture and the outcomes for patients receiving ECMO, and also reviewed the literature concerning the consequences of secondary hematogenous infection during cardiopulmonary support, as well as related prevention measures.[11] Hsu et al.[12] studied patients receiving ECMO support therapy for a period in excess of 72 h, between 2001 and 2007, to investigate the incidence rate and the risk factors of ECMO-related NIs. Results obtained from the patients' ECMO conventional data, infection-related clinical symptoms, and laboratory assays revealed that ECMO duration and the length of time spent in the Intensive Care Unit (ICU) were the highest risk factors in the development of NI. The duration of ECMO support was the only independent risk factor. Although previous studies have assessed the risk factors of ECMO-related NIs using clinical data, analysis of aspects of phenotypic drug-resistance and protein levels have seldom been described. Alongside medical developments over time, the risk factors and pathogens of NI also gradually change in varying ways and in different locations. Zhongshan Affiliated Hospital had not previously investigated ECMO-related NIs; therefore, a retrospective analysis was undertaken, using clinical data from 75 ECMO patients that had been admitted into our hospital, who met the inclusion criteria, having received ECMO support therapy from January 2009 to April 2014, with the aim of investigating NI-associated risk factors.

Materials and methods

General information

The clinical data and laboratory test results of 75 patients receiving ECMO were collected from patients admitted to Zhongshan Affiliated Hospital, from the period between January 2009 to March 2014, who met the following inclusion criteria: older than 18 years of age and having had ECMO support therapy for a duration >24 h. Forty-four males (58.67%) and 31 females (41.33%) met these criteria. The ECMO modes and the auxiliary time are shown in Table 1. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Zhongshan Affiliated Hospital of Sun Yat-sen University. Written informed consent was obtained from all participants.

Setting and study population

The clinical data and test results of these 75 ECMO-NI patients were analyzed retrospectively, and the diagnoses of NI were classified referring to the "diagnostic criteria of NI (Trial)", as issued by the Ministry of Health in 2001,[13] which includes NIs that developed during the period of hospitalization. NIs acquired prior to admission, manifesting in the incubation period during hospitalization, or appearing post-hospitalization were excluded. In our study, NIs acquired during hospitalization or after discharge from hospital were included. Any NI cases that developed within the first 24–48 h of ECMO support therapy were defined as ECMO-related NIs.[14] Patients identified as having developed post-ECMO complications during the post-hospital discharge periods were divided into two groups, the NI group and the non-NI group, for the purpose of comparison and analysis. The patients included in the study comprised all the patients undergoing ECMO and meeting the inclusion criteria during the study period.

Statistical analysis

The SPSS 10.0 statistical package (SPSS Inc., Chicago IL) was used to sort the input data for the related analysis and processing. The comparison of the rates was performed using the chi-square test or the Fisher exact test; the comparison of the averages of non-normal data was performed using the rank sum test, with the test significance level set at $P > 0.05$. Multivariate analyses were performed to determine the risk factors associated with ECMO.

Results

Evaluating risk factors in ECMO

Among the 75 ECMO patients, 20 patients developed an NI, and the incidence rate of NI was 26.67%. The risk factors in the NI group and the non-NI group were then analyzed, and the results revealed that NI was related to an extended duration of ECMO support therapy and an increased length of hospital stay, and the differences were statistically significant ($P < 0.05$). The average hospital stay for the NI group was longer than for the non-NI group ($P < 0.05$), and the ratio of patients receiving >48 h ECMO in the NI group was higher than that of patients in the non-NI group ($P < 0.05$). There was no significant difference in age, sex, ECMO mode, sternal infection, invasive interventions, antibiotic use, or hormone treatment between the two groups ($P > 0.05$, Table 1).

Main pathogens, sources of infection, and drug susceptibility in the ECMO-NI patients

A total of 58 strains of pathogens were identified in samples collected from 20 infected patients, which were mainly gram-negative bacilli such as *Acinetobacter baumannii* (21 strains) and *Pseudomonas aeruginosa* (18 strains); gram-positive cocci were the next most common, mainly including *Staphylococcus epidermidis* and *Staphylococcus aureus*. The post-ECMO infections involved mainly