BIBLIOGRAPHIC INFORMATION SYSTEM

Journal Full Title: Journal of Biomedical Research & Environmental Sciences

Journal NLM Abbreviation: J Biomed Res Environ Sci

Journal Website Link: https://www.jelsciences.com

Journal ISSN: 2766-2276

Category: Multidisciplinary

Subject Areas: Medicine Group, Biology Group, General, Environmental Sciences

Topics Summation: 128

Issue Regularity: Monthly

Review Process type: Double Blind

Time to Publication: 7-14 Days

Indexing catalog: Visit here

Publication fee catalog: Visit here

DOI: 10.37871 (CrossRef)

Plagiarism detection software: iThenticate

Managing entity: USA

Language: English

Research work collecting capability: Worldwide

Organized by: SciRes Literature LLC

Manuscript should be submitted in Word Document (.doc or .docx) through

Online Submission

form or can be mailed to support@jelsciences.com

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JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
issn: 2766-2276
SUBJECT AREA(S): BIOMEDICAL ENGINEERING
DOI: 10.37871

REVIEW ARTICLE

Use of Biomaterials in Endotracheal Tubes: Perspective under Optica of Infectology

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ABSTRACT

Biomaterials are strategies that allow researchers to expand the investigative aspects and identify potential for the composition of objectives for clinical use. This study aims to evaluate the use of biocompounds with antimicrobial action as an alternative in the coating of endotracheal tubes. The methodology used was a narrative review of the bibliography. To this end, the northern question was elaborated according to the PICo strategy. The databases consulted were: PubMed, Embase, Lilacs; using the descriptors: Biomaterial, Biopolymer, Polymer, Endotracum tube, Mechanical ventilation, Orotracqueal tube, Pneumonia, Pneumonia associated with mechanical ventilation. Reports of relevant activity of biocompounds against biofilm-making pathogens were observed inside the tubes, especially *Pseudomonas aeruginosa, Staphylococcus aureus and Staphylococcus pneumoniae*. Thus, the results obtained report a new perspective from the point of view of prevention and combating infections associated with endotracheal intubation, which is an alternative for the construction of hospital objects with antimicrobial action.

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DOI: 10.37871/jbres1692

Submitted: 03 March 2023

Accepted: 13 March 2023

Published: 16 March 2023

Introduction

Endotracheal Intubation Tubes (EIT) are devices often used in intensive care, especially for patients with severe airway diseases [1]. However, the use of this device has great potential for bacterial infections in the sick. This risk is justified because it is an invasive procedure, and since PVC - material used for tube composition - is directly in contact with the patient's mucosa, there is an increase in airway irritation [2].

The inflammatory process caused, generates above average secretions, and can evolve to laryngeal edema, ulcerations and vocal cord detriments, which makes this environment conducive to the proliferation of bacteria, both endogenous and exogenous. According to this scenario, the scientific literature warns about a direct relationship of mechanical ventilation with the genesis of injuries and infections, especially pneumonia, given that individuals submitted to the Orotracheal Intubation (OTI) process commonly enjoy this mechanism for a prolonged time [3].

In this sense, it is observed that this lung disease is one of the most frequent in hospitals and, one of the most reported infections in the use

BIOLOGY GROUP
BIOMEDICAL ENGINEERING
VOLUME: 4 ISSUE: 3 - MARCH, 2023

How to cite this article: de Mendonça Bisneto OI, Almeida HMDS, Ferreira SB. Use of Biomaterials in Endotracheal Tubes: Perspective under Optica of Infectology. 2023 Mar 16; 4(3): 434-439. doi: 10.37871/jbres1692, Article ID: JBRES1692, Available at: https://www.jelsciences.com/articles/jbres1692.pdf

of biomaterials [3]. In fact, Ventilator-Associated Pneumonia (VAP) presents a major problem for public health, due to increased spending on hospitalizations, prolonged length of stay of the patient in the hospital and a high number of mortality [4].

In this bias, the worsening of infections caused by bacteria, fungi and multidrug-resistant protozoa, and capable of forming biofilms inside the Endotracheal Tube (ETT), require a new approach in the context of the development of new prototypes, which are capable of preventing the proliferation of these pneumatic pathogens.

Among alternatives, several studies point to the manufacture of biomaterials with antimicrobial action, such as a new silver-coated endotracheal tube, antibacterial nanocomposite and antifouling [5]. At this juncture, it is observed that these new products coated or composed of biomaterials are capable of fighting pathogens related to pulmonary infection [5].

Biocompounds are attractive alternatives for the production of endotracheal tubes, since they generally present broad antibiotic activity, as reported in investigations with essential extracts and oils of different plant types [1]. In this perspective, the need for research envisioning the development and application of these strategies as prophylactic and treatment methods is exalted, as well as for reviewing and exposing data already published on the theme.

Thus, the present study aims to describe the potential of endotracheal tubes coated with substances as their application in the prophylaxis of pulmonary infections. With this, reveal new possibilities in the development of medical materials, envisioning supporting prevention strategies and the treatment of lung diseases so frequent in recent years.

Methodology

Characterization of the study

To achieve the proposed objective, the narrative review of the scientific literature was adopted as methodological device. Thus, the study takes a qualitative, descriptive approach that explores the scientific bibliography to expose a theme. The analysis performed had as priority the capture of the most relevant data already published, for a critical and objective presentation of the findings.

The conception of the state of the art on the chosen theme occurred from a broad search, subsidized by the protocol mentioned by Almeida HMDS, et al. [6]. The genesis of this route occurred from the preparation of the guiding question, which served as a guide to make up the results. For this purpose, the acronym PICo, corresponding to population/interest/context of the research in question, was used.

Conducting the investigation

The present study raised the question: "What effect does the endotracheral tubes coated with biomaterials (P) as an antibiotic therapeutic strategy (I), considering cases of pneumonia (Co)?" Furthermore, the investigation began during the months of January and February 2023 in online repositories for scientific articles, such as PubMed, Embase, Lilacs. Thus, combined descriptors were used in the following search formula: ("Biomaterial" OR "Biopolymer" OR "Polymer") AND (Endotracqueal Tube OR Mechanical Ventilation OR Orotracqueal Tube) AND ("Pneumonia" OR Pneumonia associated with mechanical ventilation) AND (RCT OR randomized OR randomized OR random OR "case-control").

To perform this review, the time interval for works published in the last 5 years was determined. The selected writings expose directly in their title and abstract that their research refers to a new medical prototype coated or produced from biomaterials in order to prevent the formation of biofilms inside.

Selection parameters

This study prioritized writings published in the form of scientific articles, published in the languages: English, Spanish and Portuguese. Soon after inclusion, the studies without full results, which do not meet or were not formulated to answer the northern question of this investigation, and duplications were excluded. Finally, the selected articles were read and the most relevant information began to be highlighted in order to contemplate the purpose of this study.

Exposure of the findings and synthesis of the information

After contemplation of each work individually, the synthesis of the findings was started to correspond to the scope of the investigation. Figure 1 shows the methodological route followed. It is important to highlight that it was not necessary to resort to the judges to begin a qualitative procedure of the data

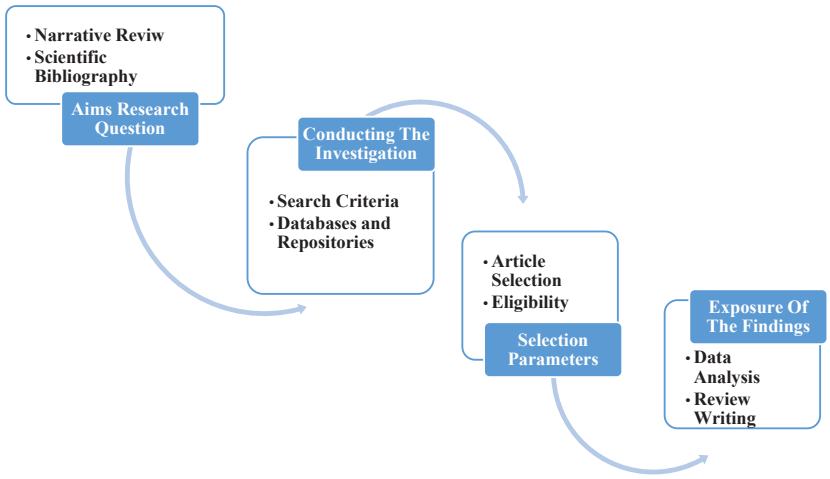

Figure 1 Methodological scheme.

obtained, nor was submission to the research ethics council, since the samples extracted are in the public domain.

Results and Discussion

Biomaterials are any substances or combinations of substances whether natural or synthetic. Its application is intended for the biomedical area with interaction in biological systems, such as prostheses and implants, being able to act replacing or separating some organic system, or treating health problems [7]. Thus, throughout its use, it was observed the possibility of application in endotrachea tubes in order to prevent the formation of bacterial biofilms.

In this bias, the importance of such compounds is understood, as it reinforces the possibility of innovations in biomedical engineering and in the health area. Thus, throughout the construction of this study, 12 articles were pre-selected, seeking to relate products coupled in endotrachea tubes, since bacterial biofilms are increasingly resistant to antibiotics: a constant concern of health researchers.

However, only seven studies answered the elaborate guide question and presented the relevance of products coupled in endotracheal tubes. Thus, these chosen works were analyzed in full, extracting the main data for a critical analysis of this issue. Conventional endotracheal tubes are a favorable environment for the proliferation of bacterial biofilms, a fact that allows the increase in mortality and morbidity in patients undergoing OTI or VAP.

Thus, the use of biomaterials, for example, silver, polyamide, gardin and gendine, applied to these tubes as an intermediary to prevent bacterial formation within this object, represents a strategy with potential for a new approach therapy [3,7]. Figure 2 shows the biomaterials for coating and their research frequency, considering the literature consulted.

The action of biomaterials with the coating function, especially compounds containing silver, is undoubtedly of fundamental importance to complaint new products with antibiotic action. It is coherent to highlight in this approach, its efficacy against fungi and bacteria, delaying the emergence of pathogens on the internal surface of endotracheal devices [3,7,9].

The investigated works presented a wide variety of antibiotic studies against several pathogens of clinical interest. Figure 3 shows the commonly studied microorganisms, being represented as to their frequency of tests.

The report by Wang Y, et al. [5], presents a ETT coated with polyacrylamide, a PAAm-Gelatin molecular chain gel. This compound presents a good hydrophilicity with strong covalent bonds and, through this mechanism, demonstrated great antimicrobial resistance and effect against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, when compared to the tubes marketed today.

The investigation by Olson ME, et al. [9], randomized and double-blind, used dogs to evaluate the influence of endotracheal tubes coated with silver hydrogel antimicrobial on pulmonary bacterial load. The control group was characterized by animals using

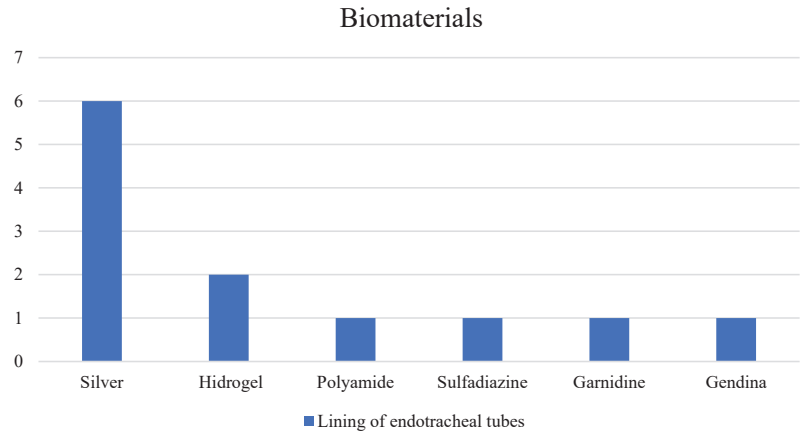

Figure 2 Frequency of investigated biomaterials.

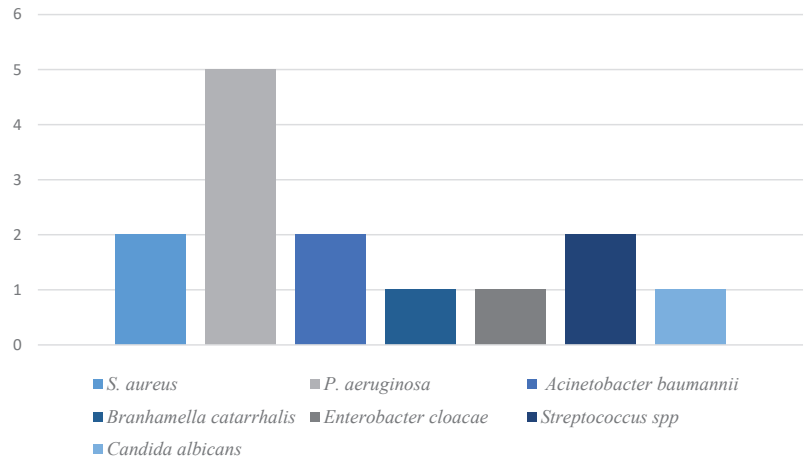

Figure 3 Frequency of investigated microorganisms.

conventional tubes and without antibiotic agents. To carry out the experiments, *Pseudomonas aeruginosa* strains were administered orally.

After tests, a higher total aerobic bacterial load was observed in the pulmonary parenchyma of dogs that used the conventional tube when compared to dogs submitted to OTI with the object coated with silver hydrogel, respectively 4.8 ± 0.8 *vs.* 5.4 ± 0.9 log cfu/g of lung tissue [9]. Differences were observed in histological and macroscopic evaluations of lung inflammation, and a scale from 0 to 12 was used to evaluate some phlogistic factors (hyperemia, edema, cellular infiltration and bacterial presence).

Dogs that used coated tubes had statistically lower scores when compared to those who used objects without silver biomaterials, 2.8 ± 1.2 *vs.* 7.1 ± 1.6, respectively [9]. These results can be justified by silver having antibiotic activity already explored in pharmacology, in addition to the hydrogel allowing a higher humidity of the site and conservation of the tissue that is in contact, preventing lesions in the respiratory tract [10].

Moreover, the study by Tokmaji G, et al. [10], with systematic review methodology, evaluated the use of coated and uncoated ETT. Intubated patients were studied in order to compare the effect of silver ion coating against conventional tubes. The results of this research found that the TTO coated with silver ions reduced the risk of developing VAP from 6.7% to only 3.5% in a period of 10 days after OTI. In addition, patients without the coated tube require mechanical ventilation for another 24 hours when compared to patients intubated with coated ETT.

In the study by Lethongkam S, et al. [11], the Polyamide/AgNP composite coating ETT promoted broad-spectrum activity against Gram-positive and Gram-negative bacteria, and proven action against *Candida albicans* and increased antimicrobial activity. The formation of biofilms by *Pseudomonas aeruginosa* and *Staphylococcus aureus*, pathogens commonly found in EIT associated with mechanical ventilation, was inhibited in 96% after intubation for 72 h.

Observing the results of Afessa B, et al. [12], randomized and with the use of patients, it was found that silver lining was associated with reduced mortality in patients with VAP about 36% when compared to the uncoated group.

In a prospective randomized, phase I-II clinical trial proposed by Berra L, et al. [13], forty-six patients were evaluated, in which twenty-three patients were intubated with a standard device (n = 23; St-ETT group, control group) and 23 with SSD-ETT coated with silver sulfadiazine (n = 23; SDD-ETT Group, study group).

SSD coating prevented bacterial colonization of the ETT. It also found that no bacterial biofilm could be found in the lumen of any SDD-ETT. In this sense, sulfadiazine-coated tubes can be safely quoted in preventing bacterial colonization in patients intubated for up to 24 h [14].

In addition, Issam I, et al. [14], evaluated the gardin coating, obtaining a result of complete inhibition of biofilm formation by *P. aeruginosa, A. baumannii, S. pneumonia* and *E. cloacae* compared to conventional ETT. In the same study, it was verified that the formation of fungal biofilms by *C. albicans* was also completely inhibited in gardin coatings. The investigations also explored a comparison between gardin-coated tubes with silver-coated tubes, regarding the potential for inhibition of biofilms. It was then revealed that gardin has greater efficacy than silver as to make it impossible to form biofilms [14].

Thus, the literature exalts the importance of research focusing on the development of functional tubes, which in addition to enabling endotracheal ventilation, also enable the prevention and treatment of infectious diseases.

Conclusion

Due to their versatility and multiplicity, biomaterials are an important possibility to make tubes with antibacterial action. Furthermore, studies demonstrate the importance of using this new process in several areas of knowledge. Moreover, it is important to highlight that these compounds showed activity of great importance and impact against resistant pathogens and biofilm formers inside endotracheal tubes, such as *Pseudomonas aeruginosa, Staphylococcus aureus and Streptococcus pneumoniae.*

The present study aims to expand alternative means for the development of new medical prototypes associated with biomaterials. However, there is a demand for more research that provides the use of other compounds with antibacterial action to serve as a coating for these devices, such as the exploration of products of natural origin, such as extracts and vegetable oils.

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How to cite this article: de Mendonça Bisneto OI, Almeida HMDS, Ferreira SB. Use of Biomaterials in Endotracheal Tubes: Perspective under Optica of Infectology. 2023 Mar 16; 4(3): 434-439. doi: 10.37871/jbres1692, Article ID: JBRES1692, Available at: https://www.jelsciences.com/articles/jbres1692.pdf