



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to Editors



Bioluminescence and ventilator-associated pneumonia caused by oral biofilm in ICU during COVID-19 -Is there a possible relationship?

ARTICLE INFO

Keywords

Bioluminescence.
 COVID-19.
 ICU deaths
 Ventilator-Associated Pneumonia

ABSTRACT

Ventilator-associated pneumonia (VAP) has been claiming many lives in the intensive care unit (ICU) during COVID-19. Oral biofilm and bacterial contamination that can be passed on from the oral cavity to the lungs during endotracheal intubation has been found to be the main culprit. Bioluminescence-based assays are emerging as potential clinical diagnostics methods. Hence, we hypothesize that the bioluminescent imaging technique can be used in the ICU to determine the load of biofilm-associated with patients undergoing endotracheal intubation. Early detection of such infections and their management can effectively bring down mortality and influence the death rate in ICU caused due to VAP. Government agencies and policymakers should be made to take this issue of deaths in the ICU due to VAP more seriously and act judiciously to methods such as bioluminescence based on sound scientific evidence.

Sir,

Ventilator-associated pneumonia (VAP) is a global concern as it is associated with higher morbidity, mortality, intensive care unit (ICU) stay, and escalates healthcare costs [1]. During the COVID-19 pandemic, the widespread use of invasive mechanical ventilation to ease acute respiratory distress (ARD) has exposed many patients to VAP risk. The lung disease in SARS-CoV-2 is adversely affected by the presence of other co-infections, virulent oral microbiota disseminated into the lower respiratory tract, and altered immunoinflammatory response [2], which can either lead to permanent damage or accelerated cellular senescence [3]. Reduction in host mechanisms such as coughing, mucociliary clearance, impaired phagocytosis by neutrophils, the elevation of regulatory T-cells, and monocyte deactivation are also reported [4]. Aspiration of oral-gastric contents, microbial biofilm development on the endotracheal tube, lung hypoxia, and often poor oral hygiene is often found to be leading causes of VAP in ICU patients [5,6]. Therefore, poor oral hygiene significantly increases the risk of pneumonia [7].

Bioluminescence-based assays are emerging as a promising clinical diagnostics method in such cases [8,9]. This can be done by introducing genetically engineered oral bacteria into the biofilm used for real-time bioluminescent imaging. Recombinant bioluminescent bacteria can detect the low levels of light emitted from bioluminescent pathogenic oral bacteria utilizing a charge-coupled device (CCD) camera. However, since there is a need for oxygen for bioluminescent reactions, the validity of bioluminescent imaging for anaerobic bacteria associated with mature plaque needs to be studied.

This pandemic has considerably increased the number of patients needing ventilator machines, and patients in the ICU on ventilators have a higher oral bacterial burden. Based on the increased incidence of VAP in ICU and the potential of bioluminescent imaging to identify oral biofilm, it can be hypothesized that the bioluminescent imaging technique can be used in the ICU to determine the load of biofilm-associated with VAP. While evaluating this hypothesis, we propose that a non-

invasive technology such as bioluminescent imaging can be used routinely to control the mortality caused by COVID-19 infections in a practical way. Application of bioluminescence in identifying the degree of bacterial load in chronically ill and intubated patients should be encouraged as it can be a means to save many lives by early detection of contamination. Government agencies and policymakers should be made to take this issue of deaths in the ICU due to VAP more seriously and act judiciously to methods such as bioluminescence based on sound scientific evidence.

Contributors

LS put forward the hypothesis. BJ and LS did the literature search. BJ drafted the paper. LS revised the manuscript and provided ideas about the mechanism of Bioluminescence and Ventilator-associated pneumonia.

Funding

Funding not received for the study.

Consent statement/ethical approval

Not required.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The author LS holds IP rights and touches royalties.

<https://doi.org/10.1016/j.mehy.2021.110760>

Received 10 June 2021; Received in revised form 23 November 2021; Accepted 6 December 2021

Available online 3 January 2022

0306-9877/© 2022 Elsevier Ltd. All rights reserved.

References

- [1] Kollef MH, Chastre J, Fagon J-Y, François B, Niederman MS, Rello J, et al. Global prospective epidemiologic and surveillance study of ventilator-associated pneumonia due to *Pseudomonas aeruginosa*. *Crit Care Med* 2014;42(10):2178–87. <https://doi.org/10.1097/CCM.0000000000000510>.
- [2] Bao L, Zhang C, Dong J, Zhao L, Li Y, Sun, J, Oral Microbiome and SARS-CoV-2: Beware of Lung Co-infection. *Front Microbiol* 2020;11:1840. <https://doi.org/10.3389/fmicb.2020.01840>.
- [3] Aquino-Martinez R, Hernández-Vigueras S, Hernández-Vigueras, S, Severe COVID-19 Lung Infection in Older People and Periodontitis. *J Clin Med* 2021;10(2):279. <https://doi.org/10.3390/jcm10020279>.
- [4] Li X, Kolltveit KM, Tronstad L, Olsen I. Systemic diseases caused by oral infection. *Clin Microbiol Rev* 2000;13(4):547–58. <https://doi.org/10.1128/CMR.13.4.547-558.2000>.
- [5] Saensom D, Merchant AT, Wara-aswapati N, Ruaisungnoen W, Pitiphat W. Oral health and ventilator-associated pneumonia among critically ill patients: a prospective study. *Oral Dis* 2016;22(7):709–14. <https://doi.org/10.1111/odi.12535>.
- [6] Wang, H., M, Y., Y, J., C, B., D, J., Y, L., O, C., Incidence Rates, Risk Factors, and Mortality Rates of Ventilator-Associated Pneumonia: A systematic Review and Meta-analysis. (2020) <https://doi.org/10.21203/rs.2.20681/v1>.
- [7] Nakajima Masato, Umezaki Yojiro, Takeda Satoshi, Yamaguchi Masahiro, Suzuki Nao, Yoneda Masahiro, et al. Association between oral candidiasis and bacterial pneumonia: A retrospective study. *Oral Dis* 2020;26(1):234–7. <https://doi.org/10.1111/odi.v26.110760>.
- [8] Frank LA, Krasitskaya VV. Application of enzyme bioluminescence for medical diagnostics. *Adv Biochem Eng Biotechnol* 2014;144:175–97. https://doi.org/10.1007/978-3-662-43385-0_6.
- [9] Hu X, Cai Y, Wang Y, Wang R, Wang J, Zhang B. Imaging of bioluminescent *Klebsiella pneumoniae* induced pulmonary infection in an immunosuppressed mouse model. *J Int Med Res* 2020;48. <https://doi.org/10.1177/0300060520956473>. 0300060520956473.

Betsy Joseph^{a,*}, Liviu Steier^{b,c}

^a Department of Periodontics, Saveetha Dental College and Hospitals, Saveetha University, Chennai 600077, India

^b Department of Preventive and Restorative Sciences, School of Dental Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA.

^c Department of Restorative Dentistry, Saveetha Dental College and Hospitals, Saveetha University, Chennai 600077, India

* Corresponding author.

E-mail address: jobets121@gmail.com (B. Joseph).