Search for biomarkers in critically ill patients: a new approach based on nuclear magnetic resonance spectroscopy of mini-bronchoalveolar lavage fluid

Chandan Singh1,2, Ratan Kumar Rai1, Afzal Azim3*, Neeraj Sinha1* and Arvind Kumar Baronia3

Human lungs have the function of gas exchange in the body, performed efficiently by the unique anatomy of the alveoli. The alveolar epithelial lining fluid, reflecting a snapshot of molecular events happening there, can be extracted by bronchoscopic/nonbronchoscopic methods and used to study critical diseases. Although there are methods to study the pathophysiological conditions, there is still a need for newer and faster methods that can provide metabolic information about disease diagnosis, severity and progression.

In this letter we present nuclear magnetic resonance-based metabolomics (a key component of system biology), which has potential for disease diagnosis and treatment monitoring [1].

Acute respiratory distress syndrome (ARDS) is a disease with a high rate of mortality and morbidity worldwide, survival being only up to 40%. There is immense need for biomarkers associated with ARDS, and scientists have been working hard for the last four decades to discover these, without the anticipated success. Bronchoalveolar lavage fluid, mini-bronchoalveolar lavage (mBAL) fluid and serum have been the primary body fluids studied for this purpose. Recently, our group explored small molecular weight metabolites responsible for severity of ARDS, employing metabolomics in mBAL fluid and serum [2,3]. Both bronchoalveolar lavage fluid and mBAL fluid can also be used for nuclear magnetic resonance-based metabolomics [4].

We used a nonbronchoscopic, catheter inside catheter technique to extract mBAL fluid [5]. Most of the metabolites were characterized and identified (Figure 1). The branch-chain amino acid, lactate, alanine, lysine, arginine, acetate, succinate, taurine, phenylalanine, betaine and aspartate levels were elevated in the mBAL fluid collected from a diseased patient compared with that from a healthy control (Figure 1). The proline level was found to decrease in the case of ARDS. The roles of the above-mentioned small molecular weight metabolites have been discussed previously [2]. One-dimensional nuclear magnetic resonance spectra can be preprocessed and utilized for unsupervised and supervised chemometric analysis, highlighting the role of key metabolites. Jelly should be avoided during extraction of mBAL fluid because resonance from it dominates the spectrum and masks resonance from small molecular weight metabolites, as shown in Figure 1. We have summarized the complete procedure in Figure 2 and in detail in one of our earlier studies [2].

With precautions, researchers will find application for this procedure in the study of diseases such as respiratory failure, interstitial lung disease, sarcoidosis and so forth. Besides the above-mentioned studies, this will be of extreme importance for clinicians as well as basic scientists trying to obtain more information about diseases where the balance of bronchoalveolar lavage fluid is affected.

*Correspondence: draazim2002@gmail.com; neeraj.sinha@cbmr.res.in
1Department of Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India
2Centre of Biomedical Research, Sanjay Gandhi Postgraduate Institute of Medical Sciences Campus, Raibarely Road, Lucknow 226014, India
3Department of Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India
Full list of author information is available at the end of the article

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Abbreviations
ARDS: acute respiratory distress syndrome; mBAL: mini-bronchoalveolar lavage.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
CS and RKR carried out sample collection, performed nuclear magnetic resonance analysis and wrote the manuscript. NS and AA designed the work. AA and AKB performed extraction of mBAL fluid from the patients. All authors read and approved the final version of the manuscript.

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Author details
1Centre of Biomedical Research, Sanjay Gandhi Postgraduate Institute of Medical Sciences Campus, Raibarely Road, Lucknow 226014, India. 2School of Biotechnology, Faculty of Science, Banaras Hindu University, Varanasi 221005, India. 3Department of Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India.

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References
1. Beckonert O, Keun HC, Ebbels TMD, Bundy J, Holmes E, Lindon JC, Nicholson JK: Metabolic profiling, metabolomic and metabonomic procedures for NMR spectroscopy of urine, plasma, serum and tissue extracts. Nat Protoc 2007, 2:2692–2703.
2. Rai RK, Azim A, Sinha N, Sahoo J, Singh C, Ahmed A, Saigal S, Baronia A, Gupta D, Gurjar M, Poddar B, Singh RK: Metabolic profiling in human lung injuries by high-resolution nuclear magnetic resonance spectroscopy of bronchoalveolar lavage fluid (BALF). Metabolomics 2013, 9:667–676.
3. Singh C, Rai R, Azim A, Sinha N, Ahmed A, Singh K, Kayastha A, Baronia AK, Gurjar M, Poddar B, Singh R: Metabolic profiling of human lung injury by 1H high-resolution nuclear magnetic resonance spectroscopy of blood serum. Metabolomics 2014. [Epub ahead of print].
4. Singh C, Rai R, Azim A, Sinha N, Ahmed A, Singh K, Kayastha A, Baronia AK, Gurjar M, Poddar B, Singh R: Mini-bronchoalveolar lavage fluid can be used for biomarker identification in patients with lung injury by employing 1H NMR spectroscopy. Crit Care 2013, 17:430.
5. Khilnani GC, Arafa K, Hadda V, Kapil A, Sood S, Sharma SK: Comparison of bronchoscopic and non-bronchoscopic techniques for diagnosis of ventilator associated pneumonia. Indian J Crit Care Med 2011, 15:16–23.

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