CRITICAL CARE

LETTER

Mini-bronchoalveolar lavage fluid can be used for biomarker identification in patients with lung injury by employing ^{1}H NMR spectroscopy

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Acute respiratory distress syndrome (ARDS) is a serious lung injury and has low survival rates. More than 150,000 cases of ARDS are diagnosed every year in the US alone, according to the National Heart, Lung, and Blood Institute database. ^{1}H nuclear magnetic resonance (NMR) has been a well-established technique for the recognition of biomarkers in various body fluids [1]. Over last few decades, investigators have searched for novel biomarkers for the diagnosis and prognosis of patients with lung injury [2]. Bronchoalveolar lavage (BAL) fluid has been used for years for diagnosis and prognosis of lung injury and related pulmonary diseases by means of various techniques [2]. BAL fluid is favored over mini-bronchoalveolar lavage (mBAL) for diagnostic as well as research purposes since the former is extracted from the immediate vicinity of alveoli. mBAL requires that fluid be taken from proximal alveoli and bronchi but can provide information about biochemical events happening inside the lungs. In this letter, we show, via ^{1}H NMR spectroscopy, that small metabolites present in BAL fluid and mBAL fluid are similar and can be used for metabolomic-related studies [3]. NMR spectroscopy of BAL has been used for metabolomic analysis of cystic fibrosis [4]. ^{1}H NMR spectroscopy of mBAL fluid can be used for other prospective studies such as those that are conducted to differentiate between infective (pulmonary) and inflammatory (non-pulmonary) ARDS and to determine the type of microbial infection associated with them [5,6]. Though extracted from a different location, mBAL fluid has small metabolites similar to those of BAL fluid. This is shown in Figures 1a and 1b, which depict one-dimensional and two-dimensional NMR spectra of BAL fluid and mBAL fluid, which are represented by red and black colors, respectively. Qualitatively, only choline metabolite, which is present in mBAL fluid and absent in BAL fluid, is different. Quantitatively, most of the metabolite resonances had similar intensities. In a recently published article, we showed that by combining ^{1}H NMR spectroscopy of mBAL fluid with multivariate statistical analysis, we can clearly differentiate between patients with lung injury and healthy controls [7]. In this first report of ^{1}H NMR of mBAL fluid, we showed an association of small metabolites with severity of infection. Taurine and threonine levels were found to be elevated in cases of ARDS, and have been correlated to severity of infection earlier. Additionally, concentrations of leucine, valine and isoleucine (muscle breakdown products), arginine, glycine, aspartic acid, succinate, acetate, and glutamate were elevated and proline level was found to be decreased in cases of ARDS. Hence, on the basis of our results, we conclude that mBAL fluid combined with ^{1}H NMR spectroscopy can be used for diagnosis and prognosis of ARDS and its severity.

Abbreviations

ARDS, acute respiratory distress syndrome; BAL, bronchoalveolar lavage; mBAL, mini-bronchoalveolar lavage; NMR, nuclear magnetic resonance.

Competing interests

The authors declare that they have no competing interests.

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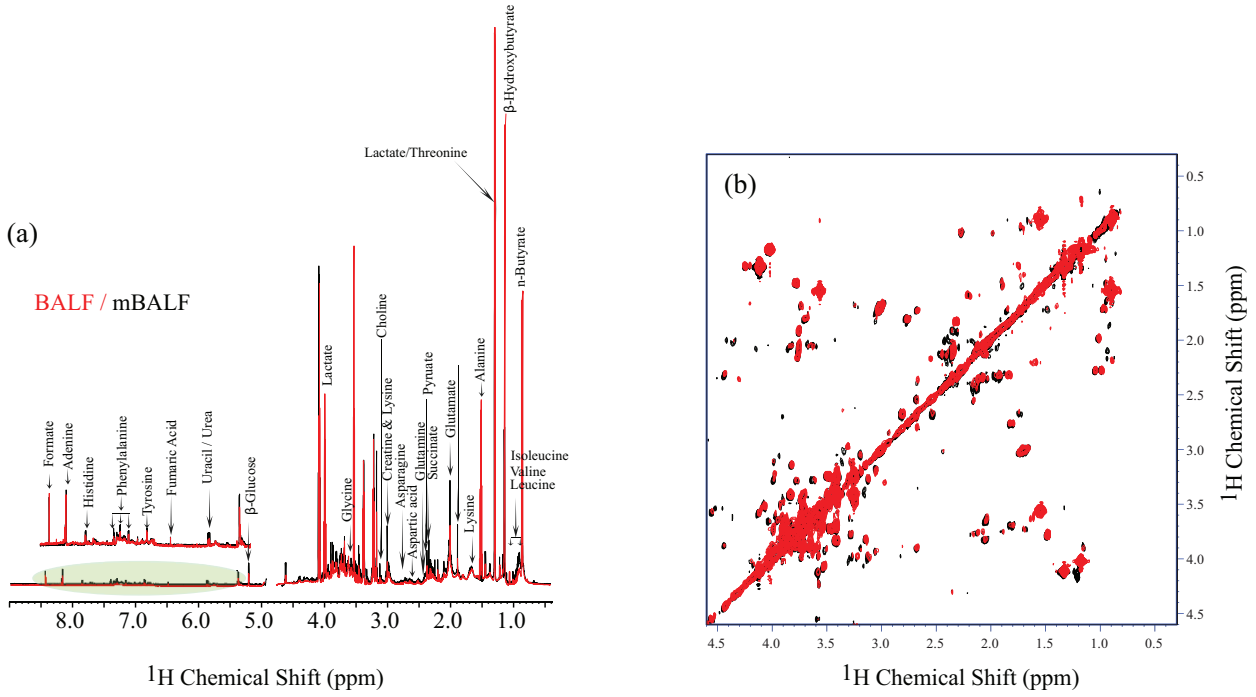

Figure 1. One-dimensional (a) and two-dimensional (b) ^{1}H nuclear magnetic resonance spectrum of bronchoalveolar lavage fluid (BALF) (red) and mini-BALF (mBALF) (black). Peaks corresponding to various small molecular weight metabolites were identified and are shown in the figure. ppm, parts per million.

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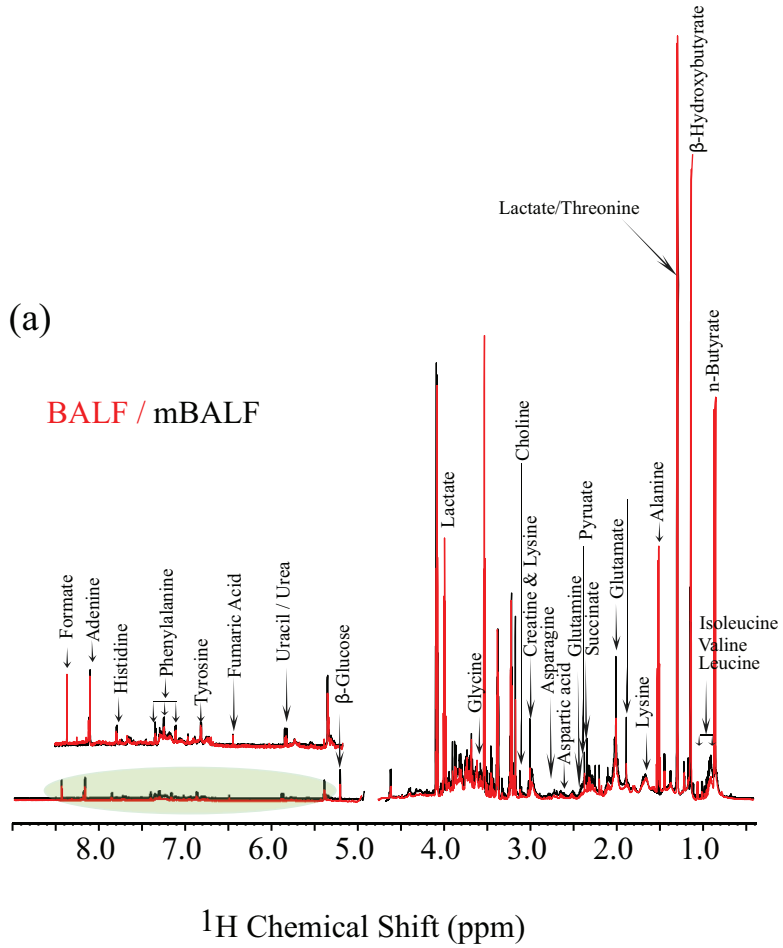
(a)
BALF / mBALF
Formate
Adenine
Histidine
Phenylalanine
Tyrosine
Fumaric Acid
Uracil / Urea
β-Glucose
Lactate
Glycine
Creatine & Lysine
Asparagine
Aspartic acid
Glutamine
Succinate
Glutamate
Lysine
Choline
Pyruate
Alanine
Lactate/Threonine
β-Hydroxybutyrate
n-Butyrate
Isoleucine
Valine
Leucine
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
1H Chemical Shift (ppm)

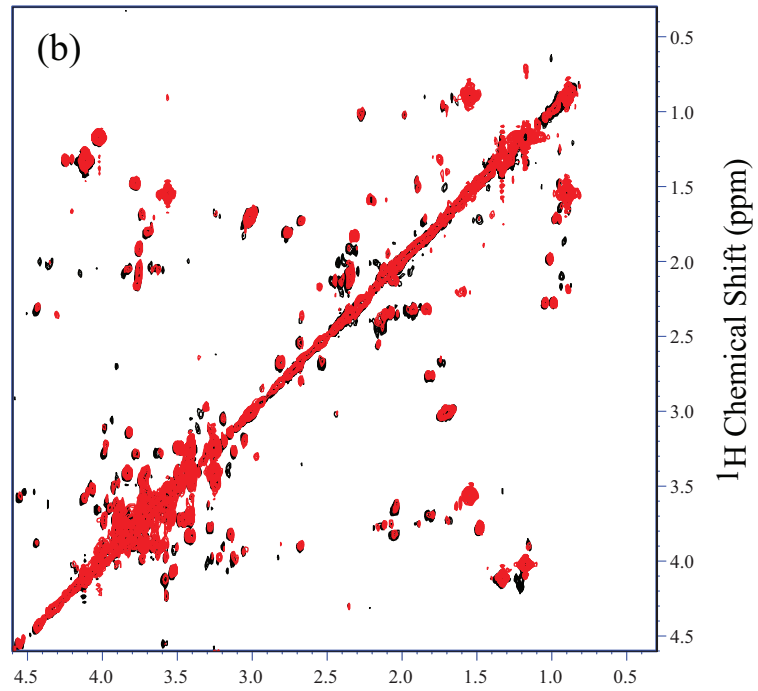
(b)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
1H Chemical Shift (ppm)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1H Chemical Shift (ppm)

Figure 1