Protective effect of endogenous β-adrenergic tone on lung fluid balance in acute bacterial pneumonia in mice

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Su, Xiao, Laurent Robriquet, Hans G. Folkesson, and Michael A. Matthey. Protective effect of endogenous β-adrenergic tone on lung fluid balance in acute bacterial pneumonia in mice. Am J Physiol Lung Cell Mol Physiol 290: L769–L776, 2006. First published November 11, 2005; doi:10.1152/ajplung.00334.2005.—Some investigators have reported that endogenous β-adrenoceptor tone can provide protection against acute lung injury. Therefore, we tested the effects of β-adrenoceptor inhibition in mice with acute Escherichia coli pneumonia. Mice were pretreated with propranolol or saline and then intratracheally instilled with live E. coli (107 colony-forming units). Hemodynamics, arterial blood gases, plasma catecholamines, extravascular lung water, lung permeability to protein, bacterial counts, and alveolar fluid clearance were measured. Acute E. coli pneumonia was established after 4 h with histological evidence of acute pulmonary inflammation, arterial hypoxemia, a threefold increase in lung vascular permeability, and a 30% increase in extravascular lung water as an increase in plasma catecholamine levels. β-Adrenoceptor inhibition resulted in a marked increase in extravascular lung water that was explained by both an increase in lung vascular permeability and a reduction in net alveolar fluid clearance. The increase in extravascular lung water with propranolol pretreatment was not explained by an increase in systemic or vascular pressures. The increase in lung vascular permeability was explained in part by anti-inflammatory effects of β-adrenoceptor stimulation because plasma macrophage inflammatory protein-2 levels were higher in the propranolol pretreatment group compared with controls. The decrease in alveolar fluid clearance with propranolol was explained by a decrease in catecholamine-stimulated fluid clearance. Together, these results indicate that endogenous β-adrenoceptor tone has a protective effect in limiting accumulation of extravascular lung water in acute severe E. coli pneumonia in mice by two mechanisms: 1) reducing lung vascular injury and 2) upregulating the resolution of alveolar edema.

Escherichia coli; alveolar fluid clearance; pulmonary edema; β-adrenoceptor inhibition; sodium channel

EARLIER EXPERIMENTAL WORK established that elevated endogenous epinephrine levels can increase the capacity of the alveolar epithelium to remove alveolar edema fluid in the setting of septic or hemorrhagic shock (29, 35, 36) or after an acute neurogenic insult (18). However, the effects of endogenous β-adrenoceptor tone on lung fluid balance have not been studied in acute severe bacterial pneumonia, the most common cause of clinical acute lung injury (10). We would predict that an acute elevation in endogenous epinephrine and norepinephrine levels during acute bacterial pneumonia might elevate alveolar fluid clearance by cAMP-dependent mechanisms (3, 7, 8, 16, 22–24, 33, 37), providing the alveolar epithelial barrier has not been severely damaged by the bacteria or their products. Some investigations have suggested that endogenous β-adrenoceptor stimulation may deregulate inflammatory responses and potentially protect against the development of acute lung injury (2, 32, 34).

In this study, we selected Escherichia coli because it is a common cause of gram-negative bacterial pneumonia (6, 11). The primary objective was to determine whether an acute increase in endogenous catecholamine levels favorably affected lung fluid balance and arterial blood gases during the acute phase of E. coli pneumonia. We measured plasma epinephrine levels and examined whether β-adrenoceptor inhibition by propranolol, a β-adrenoceptor antagonist, would affect the extent of pulmonary edema. Because propranolol increased extravascular lung water by both increasing lung vascular permeability and decreasing alveolar fluid clearance, we then used amiloride to inhibit epithelial sodium channels (ENaC) to determine the quantitative contribution of a decrease in alveolar fluid clearance in the absence of any effect on lung vascular permeability.

MATERIALS AND METHODS

Chemicals and reagents. Propranolol and amiloride were purchased from Sigma (St. Louis, MO). They were dissolved in 0.9% saline before each experiment. The catecholamine ELISA kit was from ImmunoBiological Laboratories (Hamburg, Germany).

Animals. For these studies, the mice (weighing 25–35 g) were housed in air-filtered, temperature-controlled units (20 ± 2°C) with food and water ad libitum. Anesthesia was induced with an intraperitoneal injection of a mixture of ketamine (90 mg/kg) and xylazine (10 mg/kg). The Committee on Animal Research of the University of California, San Francisco approved all the protocols.

E. coli preparation. E. coli serotype K1 was originally isolated from the blood of a patient with biliary sepsis. The methods used to passage, store, and amplify the bacteria have been described elsewhere (25). To count E. coli, we measured the optical density (OD) of the diluted E. coli solutions using a spectrophotometer. An equation \( Y = 4.2 \times 10^{8}X^{0.864} \) was used to calculate the numbers of E. coli (\( Y \) represents the counted number of E. coli, and \( X \) is the OD value of the diluted E. coli solution).

Acute E. coli pneumonia mouse model. A previously developed direct visualization instillation method was used to instill 105 colony-forming units (cfu) of E. coli into the air spaces of the lung (38). Briefly, the mouse was suspended with incisors attached to an ~60° wood support with 3/0 suture. A cold-light source (Dolan-Jenner Industries, Lawrence, MA) with two 25-in. flexible fiber-optic arms allowed transillumination to visualize the glottis and vocal cords to deliver the 30-μl E. coli solution via a PE-10 catheter. For an even

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distribution of the E. coli solution in the lung, the fluid instillate with E. coli was followed by 2 cmH2O pressure air inflation.

β-Adrenoceptor inhibition. To achieve significant β-adrenoceptor inhibition, we gave the mice an intrapulmonary bolus (3 mg/kg body wt) combined with an intratracheal instillation of 50 µl of 10^-4 M propranolol. The control groups were given the same amount of saline. Fifteen minutes after administration of propranolol or vehicle, the mice were intratracheally instilled with either saline or E. coli.

Sodium channel inhibition. To reduce active sodium uptake in lung epithelia, mice were intratracheally instilled with 50 µl of (10^-4 and 10^-3 M) amiloride. Control groups were given the same amount of saline. Immediately after instillation with amiloride or saline, the mice were intratracheally instilled with either saline or E. coli.

Histology. After death by halothane inhalation, the chest and abdomen were rapidly opened, and the base of the heart was clamped to prevent escape of the pulmonary blood volume. The thoracic organs were removed en bloc, and 10% formalin in was intratracheally instilled at a pressure of 25 cmH2O. After 72 h of fixation, lungs were paraffin-embedded, and 5-µm-thick sections were cut and stained with hematoxylin and eosin.

Measurement of lung wet-to-dry weight ratio. Four hours after E. coli instillation, the mice were killed by halothane inhalation. The lungs were removed, counted in a gamma counter (Packard, Meriden, CT), weighed, and homogenized. Blood was collected through right ventricle puncture. The lung homogenate was weighed, and a portion was centrifuged (12,000 rpm, 8 min) for hemoglobin concentration in lung homogenate supernatant. Another portion of homogenate, supernatant, and blood was weighed and desiccated in an oven (60°C for 24 h) for gravimetric determination of extravascular lung water. The lung wet-to-dry weight ratio was calculated as done previously (12, 31).

Measurement of lung vascular permeability. The mice were given an intrapulmonary injection of 0.05 µCi 125I-labeled albumin immediately after intratracheal E. coli instillation to determine the portion of 125I-albumin in the lung and plasma. Lung extravascular plasma equivalents (an index of lung vascular permeability) were calculated as counts of 125I-albumin in lung tissue divided by counts of 125I-albumin in plasma as performed previously (12, 31).

Measurement of blood pressure, heart rate, right atrial pressure, and arterial blood gases. Fifteen minutes before the end of the experiment, two groups of spontaneously breathing mice (saline + E. coli and propranolol + E. coli) were lightly anesthetized. Afterward, under a microscope, a PE-10 catheter (filled with heparinized saline) was inserted into the right carotid artery and connected to a Biopac data collection system (Biopac Systems, Santa Barbara, CA) via a calibrated pressure transducer to record blood pressure. Arterial blood (50 µl) was withdrawn to measure arterial blood gases with a blood gas analyzer (Diamond Diagnostics, Holliston, MA). To measure right atrial pressure, a sharpened 23-gauge plastic tubing connected with a PE-50 catheter was inserted into the isolated right jugular vein, further advanced ~1–1.5 cm, and then connected to the BIOPAC data collection system via a pressure transducer. A 3/0 suture attached to the skin was used to secure the catheter in the position. The right atrium of mice was set at the same level with the transducer.

Measurement of alveolar fluid clearance. Alveolar fluid clearance measurements were obtained 4 h after either saline or E. coli intratracheal instillation. As in our previous studies, we determined alveolar fluid clearance by measuring the increase in the protein tracer concentration (131I-albumin, 0.1 µCi) over 30 min after instillation of a 5% albumin-Ringer lactate solution (osmolality 304 mosmol/l) into the trachea using an in situ model as previously described (13). The increase in protein concentration provides a good estimate of fluid volume removed from distal air spaces of the lung (24). Briefly, mice were anesthetized with pentobarbital sodium (200 mg/kg ip) and then exsanguinated by transection of the abdominal aorta. The instillate (10–13 ml/kg, 37°C) was then instilled into the trachea. An airway pressure of 7 cmH2O was maintained for 30 min with 100% oxygen. Approximately 3–5 min after instillation, a baseline sample (50–100 µl) was aspirated from the distal airways using PE-10 tubing (time 0 sample). Thirty minutes later, a second sample was aspirated from the distal airways. Body temperature was carefully maintained at 37°C throughout the experiment with an external heating lamp and warming blanket and was monitored using a digital thermometer (Fisher Scientific, Pittsburgh, PA) placed in the abdominal cavity. Alveolar fluid clearance, expressed as a percentage of alveolar fluid volume absorbed during 30 min, was calculated using the equation:

\[ \text{Alveolar fluid clearance} = 1 - \left( \frac{P_i}{P_f} \right) \times 100\% \]

where \(P_i\) is initial 131I-albumin activity per gram at time 0 and \(P_f\) is 131I-albumin activity per gram at 30 min.

Measurement of plasma catecholamine and macrophage inhibitory protein-2. Blood was collected via puncture of the right ventricle. The plasma was stored at minus 80°C for later analysis after centrifugation (3,000 g, 5 min). Plasma epinephrine concentrations were measured using a commercial radioimmunoassay with a sensitivity of 12 pg/ml and intra- and interassay variabilities of 5 and 12%, respectively. Anti-mouse enzyme-linked immunosorbent assay kit (B&D Systems) was used for measurement of plasma macrophage inhibitory protein (MIP)-2 (interleukin 8, mouse homolog).

Lung bacterial cultures. To monitor E. coli growth, we collected and homogenized lungs from the E. coli group and propranolol + E. coli group in 1 ml of PBS. For each sample, 0.1 ml of serially diluted homogenate was inoculated on a Luria-Bertani agar plate. After 24 h of incubation at 37°C, the colonies of E. coli were counted.

Specific study groups. Specific groups were included in these studies. There were four groups in the β-adrenoceptor inhibition studies. 1) Mice in the saline + saline group were first injected intratracheally with 100 µl of 0.9% saline and intratracheally instilled with 50 µl of 0.9% saline, and then 15 min later, they were intratracheally instilled with 0.9% saline again. 2) Mice in the propranolol + saline group were injected intraperitoneally with 100 µl of propranolol (3 mg/kg body wt) and intratracheally instilled with 50 µl of 10^-4 M propranolol, and then 15 min later, they were intratracheally instilled with 0.9% saline. 3) Mice in the saline + E. coli group were first injected intraperitoneally with 100 µl of 0.9% saline and intratracheally instilled with 50 µl of 0.9% saline, and then 15 min later, they were intratracheally instilled with 10^7 cfu of E. coli in 30 µl of 0.9% saline. 4) Mice in the propranolol + E. coli group were injected intraperitoneally with 100 µl of propranolol (3 mg/kg body wt) and intratracheally instilled with 50 µl of 10^-4 M propranolol, and then 15 min later, they were intratracheally instilled with 10^7 cfu of E. coli in 30 µl of 0.9% saline.

There were three groups in the apical sodium channel inhibition studies. 1) Mice in the saline + saline group were intratracheally instilled with 50 µl of 0.9% saline and then intratracheally instilled with 30 µl of 0.9% saline. 2) Mice in the saline + E. coli group were first intratracheally instilled with 50 µl of 0.9% saline and then intratracheally instilled with 10^7 cfu of E. coli in 30 µl of 0.9% saline. 3) Mice in the amiloride + E. coli group were first intratracheally instilled with 50 µl of 0.9% saline and then intratracheally instilled with 10^7 cfu of E. coli in 30 µl of 0.9% saline.

Statistical analysis. Statistics were analyzed using SPSS software (SPSS, Chicago, IL), and results are presented as means ± SD. One-way analysis of variance (ANOVA) with Tukey’s post hoc test or Student’s t-test was used (level set at P < 0.05).

RESULTS

Acute E. coli pneumonia in mice. Mice instilled with E. coli developed respiratory acidosis (Fig. 1A), hypoxemia (Fig. 1B), and hypercparnia (Fig. 1C). Lung wet-to-dry weight ratio increased by 30% compared with saline-instilled controls (Fig. 1D). Lung histology from the E. coli-instilled group displayed...
pulmonary edema, neutrophil infiltration, hemorrhage, congestion, and consolidation (Fig. 1F). There were no pathological changes observed in the saline-instilled group (Fig. 1E).

**Plasma catecholamine levels in acute E. coli pneumonia.** There was a significant increase in plasma epinephrine levels 4 h after *E. coli* intratracheal instillation. There also was a significant increase in plasma norepinephrine levels in the *E. coli*-instilled group compared with the saline-instilled group (Fig. 2).

**Effect of β-adrenoceptor inhibition on hemodynamic parameters.** We measured systemic blood pressure and heart rate to be certain that there was a pharmacological effect of propranolol. At 4 h in the propranolol + *E. coli* group, blood pressure and heart rate were significantly lower compared with that in the saline + *E. coli* group (Fig. 3, A and B).

**Effect of β-adrenoceptor inhibition on right atrial pressure.** To be certain that cardiogenic mechanisms did not contribute to the greater quantity of lung edema in the *E. coli* group with β-adrenoceptor inhibition, we measured right atrial pressure. In control mice, mean right atrial pressure was $1.9 \pm 0.5 \text{ cmH}_2\text{O}$. In mice with *E. coli* pneumonia, the mean right atrial pressures were significantly lower than in control mice. In mice treated with propranolol, right atrial pressure was lower by another 1
cmH2O, indicating that β-adrenoceptor inhibition did not elevate atrial pressure (Fig. 4).

Effect of β-adrenoceptor inhibition on arterial blood gases in acute E. coli pneumonia. At 4 h after E. coli instillation, there was an increased acidosis (Fig. 5A), hypoxemia (Fig. 5B), and hypercapnia (Fig. 5C) in the propranolol + E. coli group compared with the saline + E. coli group.

Effects of β-adrenoceptor inhibition on E. coli growth in the lung. Because a change in the number of E. coli organisms in the two groups could potentially account for a difference in extravascular lung water, we measured E. coli counts in lung homogenate between the propranolol + E. coli group and the saline + E. coli group (Fig. 6).

Effects of β-adrenoceptor inhibition on lung edema, lung vascular permeability, and inflammatory response in acute E. coli pneumonia. After 4 h, lung wet-to-dry weight ratio in the E. coli-instilled group was significantly increased compared with that in the saline-instilled group. β-Adrenoceptor inhibition by propranolol in the E. coli-instilled group further increased the lung wet-to-dry weight ratio compared with that in the saline + E. coli group (Fig. 7A). Because β-adrenoceptor inhibition increased lung water, we first tested the hypothesis that β-adrenoceptor inhibition adversely affects lung vascular permeability. At 4 h, lung vascular permeability in the E. coli-instilled group was significantly increased compared with that in the saline-instilled group. Addition of β-adrenoceptor inhibition with propranolol in the E. coli-instilled group resulted in a further increase in lung vascular permeability compared with the saline + E. coli group (Fig. 7B). To determine whether inhibition of β-adrenergic tone had affected the inflammatory response, we measured plasma levels of MIP-2. Treatment with propranolol in the E. coli-instilled
group significantly increased plasma MIP-2 levels compared with the saline + E. coli group (Fig. 7C).

Effects of β-adrenoceptor inhibition on alveolar fluid clearance. Even though there was a marked increase in lung vascular permeability, mice with acute E. coli pneumonia did demonstrate a modest but significant increase in net alveolar fluid clearance (Fig. 8). Because elevated levels of catecholamines might have upregulated fluid transport, we tested the effect of β-adrenergic inhibition on alveolar fluid transport. Treatment with propranolol in the E. coli-instilled group significantly reduced alveolar fluid clearance compared with the saline + E. coli group (Fig. 8).

Effects of apical sodium uptake inhibition on lung fluid balance, lung vascular permeability, and alveolar fluid clearance in acute E. coli pneumonia. Because propranolol increased extravascular lung water by both worsening lung vascular permeability and decreasing alveolar fluid clearance, we thought it was important to study the effect of inhibiting alveolar fluid clearance alone. Therefore, we used amiloride, a pharmacological inhibitor of ENaC, in these experiments.

Extravascular lung water in the amiloride + E. coli group was significantly increased at 4 h compared with that in the saline + E. coli group (Fig. 9A). There was no difference in lung vascular permeability between the amiloride + E. coli group and the saline + E. coli groups at 4 h (Fig. 9B). The elevated alveolar fluid clearance in E. coli pneumonia was inhibited by amiloride (Fig. 10).

DISCUSSION

Acute bacterial pneumonia is the most common cause of clinical acute lung injury (10). The extent and severity of bacterial pneumonia are determined by multiple factors, including the virulence of the infecting organism and the host inflammatory response. Another potentially important mechanism that may limit the severity of lung edema and respiratory failure in the acute phase of bacterial pneumonia is an elevation of endogenous plasma catecholamines.

Our prior work, as well as that of other investigators, has demonstrated that elevated levels of plasma catecholamines...
can increase the capacity of the alveolar epithelium to remove alveolar edema fluid in septic shock, hypovolemic shock, and neurogenic injury (18, 30, 35, 36). However, the effect of endogenous catecholamines in the presence of severe acute bacterial pneumonia on alveolar fluid clearance and lung fluid balance has not been well studied. One recent such study did indicate that influenza viral pneumonia can inhibit ENaC-dependent sodium transport in alveolar epithelial type II cells and also decrease amiloride-dependent alveolar fluid clearance in vivo (4). Barrier properties also may be favorably affected by endogenous catecholamines, given that some investigators have reported that endogenous β-adrenoceptor tone may have beneficial effects on lung vascular permeability in hemorrhagic shock (2, 32, 35).

Therefore, we designed these studies to generate a mouse model of acute severe bacterial pneumonia in which we could study the mechanisms that determined the quantity of lung edema and the severity of acute respiratory failure to test the hypothesis that endogenous β-adrenoceptor tone may favorably influence lung fluid balance in the acute phase of bacterial pneumonia. The results convincingly demonstrate that endogenous β-adrenoceptor tone reduces the extent of pulmonary edema in acute bacterial pneumonia in mice by two major mechanisms: a reduction in severity of lung endothelial injury and an upregulation of alveolar fluid clearance.

Acute E. coli instillation produced a rapidly developing severe pneumonia with histological evidence of interstitial and alveolar edema and inflammation combined with a marked increase in extravascular lung water and a threefold increase in lung vascular permeability. Arterial blood gases demonstrated the characteristic findings of acute respiratory failure with arterial hypoxemia, hypercapnia, and acidosis that were associated with increased plasma concentrations of epinephrine and norepinephrine. We therefore designed these studies to test the hypothesis that the acute increase in plasma catecholamine levels may reduce lung edema by both decreasing lung vascular permeability and increasing alveolar fluid clearance.

This hypothesis was tested by inhibiting endogenous β-adrenoceptor stimulation by propranolol, a β-adrenoceptor antagonist. β-Adrenoceptor inhibition worsened arterial blood gases and increased extravascular lung water in mice with acute bacterial pneumonia. As expected, the heart rate and blood pressure were lower in propranolol-treated mice, demonstrating a pharmacological effect of the propranolol treatment. There was, however, no increase in right atrial pressure, making it unlikely that the adverse effects of propranolol on lung fluid balance were mediated by an increase in lung vascular pressure. The remaining experiments were designed to determine the mechanisms that explain why endogenous β-adrenergic tone had a favorable effect on lung fluid balance in acute bacterial pneumonia.

As expected, E. coli induced pulmonary edema by increasing lung vascular permeability. In the presence of β-adrenoceptor antagonist, the severity of lung vascular permeability was worsened with a substantial increase in the quantity of extravasated plasma accumulated in lung extravascular compartments. Other investigators have reported an increase in lung vascular permeability after β-adrenoceptor inhibition in hemorrhagic shock in mice because acute inflammatory responses, such as NF-κB and cytokines responses, were upregulated (1, 2).

The concept that β-adrenoceptor stimulation, whether it was endogenous or exogenous, can reduce lung endothelial permeability has been intermittently supported by a variety of experimental models (17, 21, 27, 28) and one study in human volunteers (20), but the proof of its beneficial effect in an acute model of established severe bacterial pneumonia has not been previously demonstrated. β-Adrenoceptor stimulation may improve lung endothelial permeability (17, 27, 28) by inhibiting endothelial cell contraction and reducing intracellular gaps (19, 34). In the mouse lung epithelia, β1- and β2-adrenoceptors coexist in the proportions of 18 and 82%, respectively (14). β2-Adrenergic receptor stimulation reduces production of TNF-α and IL-6 in human macrophages (15) and suppresses lipopolysaccharide-induced lung inflammation (20, 21). Higher plasma MIP-2 levels in the propranolol group with E. coli pneumonia also suggest an exaggerated inflammatory response after inhibition of β-adrenergic receptor. Thus inhibition of β2-adrenergic receptor may contribute to the deleterious effects of propranolol on E. coli pneumonia.

In addition to increasing vascular permeability, β-adrenoceptor inhibition decreased alveolar fluid clearance. This result provides direct evidence that elevated plasma catecholamine levels in the initial phase of severe bacterial pneumonia may provide some protection by reducing the extent of alveolar edema formed. Although we previously reported that elevated endogenous epinephrine levels could increase alveolar fluid clearance in septic or hemorrhagic shock, the observations in this study are even more remarkable because they demonstrate a beneficial effect of cAMP-dependent stimulation in acutely injured lungs in the presence of a marked increase in lung vascular permeability. In our prior studies with septic or hemorrhagic shock (29, 35, 36), the lungs were not significantly injured.

In the current study, the increase in alveolar fluid clearance following intratracheal instillation of E. coli was attenuated by amiloride, indicating that the stimulation was related to an increase in sodium uptake. Thus the endogenous catechol-
amine release induces β-adrenoceptor stimulation of active sodium uptake that depends in part on ENaC in the distal airway and alveolar epithelium (9). The effect of amiloride was midway between propranolol and placebo treatment with salicylate, indicating that ~50% of the benefit of β-adrenoceptor tone was mediated by upregulated alveolar fluid clearance, whereas the other 50% was mediated by a reduction in lung endothelial permeability.

What are the clinical implications of these studies? Do these results mean that exogenous administration of aerosolized β-adrenoceptor agonists would not be necessary in critically ill patients? Because plasma catecholamine levels in ventilated patients with acute lung injury show that more than 90% of the patients have normal or only minimally elevated epinephrine levels (39), it is unlikely that there would be sufficient endogenous stimulation of the β-adrenoceptor pathway in ventilated human patients. In the usual case of acute respiratory failure from severe bacterial pneumonia, critically ill patients are sedated and given anesthetics to facilitate supportive care with positive pressure ventilation in the intensive care unit (5). In fact, the data in the current study support the concept of a potential therapeutic benefit of administering exogenous β-adrenoceptor stimulation to provide a sustained treatment of patients with acute lung injury from bacterial pneumonia. Also, one study (26) from our research group demonstrated that salmeterol treatment could reduce lung water in rats with a noninfectious cause of acute lung injury, namely, acid-induced lung injury, by both attenuating lung endothelial permeability and upregulating alveolar fluid clearance. The data in this study also suggest that in the spontaneously breathing patient who is severely ill with acute bacterial pneumonia, elevated catecholamine levels may attenuate the severity of their lung injury and pulmonary edema. However, once these critically ill patients are treated with endotracheal intubation and positive pressure ventilation, physicians use sedatives and narcotics in the vast majority of patients with acute lung injury (5). Thus the potential benefits of elevated levels of endogenous catecholamines on lung fluid balance will not persist. It is at this point in time that the patients may benefit from exogenous β2-adrenoceptor agonist therapy, either by aerosol or by the intravenous route, although this possibility will require prospective randomized clinical trials to evaluate the potential clinical benefit.

In conclusion, this study demonstrates that acute E. coli pneumonia in mice results in a marked increase in extravascular lung water, lung vascular permeability, arterial hypoxemia, and histological evidence of acute bacterial pneumonia. Because β-adrenoceptor inhibition by propranolol worsened pulmonary edema by both increasing lung vascular permeability and decreasing alveolar fluid clearance, we conclude that the acute increase in endogenous β-adrenoceptor tone may have a short-term beneficial effect on limiting the severity of lung vascular permeability as well as upregulating alveolar fluid clearance in acute E. coli pneumonia, thus limiting the extent of pulmonary edema formation.

REFERENCES


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