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Case Study

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AVIPTADIL IN ACUTE RESPIRATORY DISTRESS SYNDROME: CASE SERIES

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ABSTRACT
Acute Respiratory Distress Syndrome (ARDS) is a severe medical condition caused due to direct or indirect lung injuries with the highest rate of mortality. Aviptadil is a synthetic form of human vasoactive intestinal peptide and has been used to treat various lung inflammatory conditions, including ARDS. Aviptadil exerts an anti-cytokine effect and increases surfactant production which helps to improve the oxygenation index in ARDS patients. Our case series highlights the role of Aviptadil in the reduction of oxygen requirement and increase in PaO_2:FiO_2 ratio in moderate to severe ARDS patients.

KEYWORDS: Aviptadil, ARDS, PaO_2:FiO_2 ratio.

BACKGROUND

Acute Respiratory Distress Syndrome (ARDS) is a severe, life-threatening lung condition characterized by fluid accumulation in the alveoli in the lungs, leading to reduced oxygen exchange and difficulty breathing. Symptoms of ARDS include shortness of breath, rapid breathing, and low oxygen levels. ARDS can be a medical emergency and may require prompt treatment in a hospital setting, including high-flow oxygen, mechanical ventilation and other supportive measures. Despite advances in understanding the pathophysiologic cascade that results in ARDS, the mortality from ARDS remains high.

Aviptadil, a synthetic form of human vasoactive intestinal peptide (VIP) gets highly localized in the lungs (70%). Its clinical effects on sarcoidosis, asthma, and primary pulmonary hypertension, ARDS have been assessed.[1-7] Aviptadil is approved 'For the treatment of patients with severe COVID-19 with acute respiratory distress syndrome' in India.[8] Internationally, in the USA and European Union, this product is approved as an orphan drug designation for Acute Respiratory distress syndrome, acute lung injury, pulmonary arterial hypertension and sarcoidosis.[9-13]

In this article, we report a case series of five patients with moderate to severe ARDS (as per berlin definition) treated with Aviptadil Infusion. Aviptadil infusion at 0.166/0.332/0.498 mcg/kg/hr rate for 12 hours was administered for 3 consecutive days.

Case Report 1

Male patient aged 50 years, exposed to smoking for 2 years (1-2 cigarettes per day), with no particular pathological history. He presented with ARDS due to pneumonia at the emergency department of Gadag Institute of Medical Sciences, Gadag, Karnataka, India with 2 days of fever and cough with one day of shortness of breath. The patient reported dyspnea both at rest and upon exertion. On admission, the patient was in respiratory distress and was not able to maintain oxygen saturation on room air. The measured SpO2 was 72% at room air. The patient was transferred to the Intensive Care Unit (ICU) for further management under the medicine department. His X-ray showed heterogeneous opacities in the left middle lobe and bilateral lower lobes. The patient's arterial blood gas values analysis revealed severe ARDS. The diagnosis of left middle lobe bronchopneumonia with ARDS was confirmed, and the patient was put on mechanical ventilation support, broad-spectrum antibiotics (Inj. Meropenem infusion) and other supportive therapy.

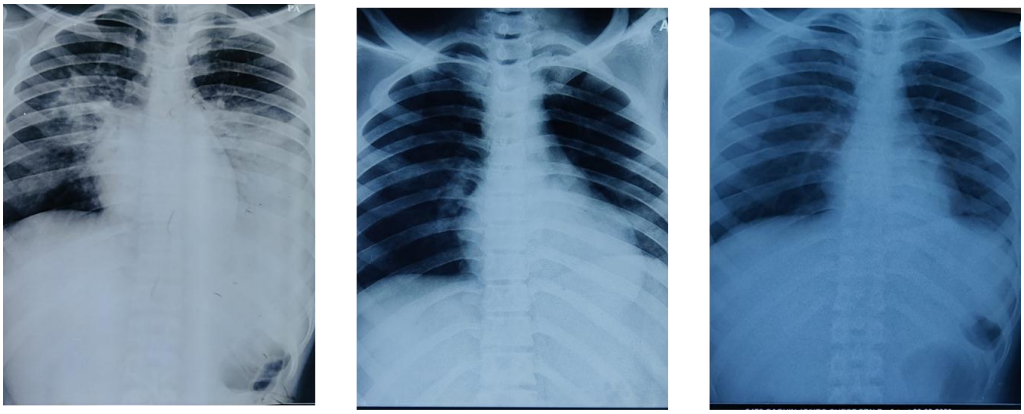
On day 2, the same treatment strategies were continued without much improvement in the patient's overall outcome. The microbiological examinations (sputum) revealed gram-positive cocci in chains suggesting *streptococcus pneumonia* infection. Considering gram-positive coverage, antibiotic therapy was escalated to injection linezolid, in addition to ongoing treatment. Despite this therapy for 2 days, the patient developed worsening hypoxemic respiratory failure. Further deterioration of gas exchange prompted the decision to intubate and mechanical ventilation via an endotracheal intubated tube.

The above-mentioned treatment was continued without much improvement in respiratory distress.

On Day 4, the PaO2/FiO2 ratio of the patient was 108 mmHg. It was planned to add Aviptadil to the ongoing therapy. Aviptadil infusion was started at a dose of 0.166 mcg/kg/day for 12 hours along with ongoing treatment and supportive care. After completion of 1st infusion, arterial blood gases reports showed a slight improvement patient's oxygenation status, acid–base balance and patient's dependence on the ventilator. The fraction of inspired oxygen (FiO2) was reduced to 80%.

The oxygenation improved after the second Aviptadil infusion at a dose of 0.332 mcg/kg/day for 12 hours and the patient was weaned off the ventilator to CPAP (continuous positive airway pressure). The patient tolerated continuous positive airway pressure (CPAP) well without evidence of respiratory distress. He maintained oxygen saturation without any signs of respiratory distress.

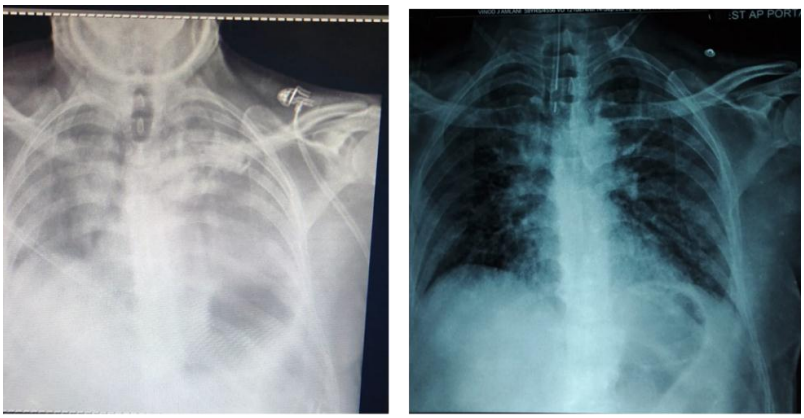
On Day 6, after the completion of 3rd infusion (0.498 mcg/kg/hr for 12 hr), the patient was stable and maintained oxygen saturation on room air. The PaO_2:FiO_2 ratio of the patient was 482 mmHg. The patient was weaned off from the CPAP and shifted to 2 liters of oxygen via nasal prongs. The patient's radiological improvement was observed for the next 48 hours and discharged from the ICU. The patient recovered well with no complications and was discharged from the hospital on room air in excellent medical condition on the 5th day following the first Aviptadil infusion.



Before Aviptadil Treatment | After Aviptadil Treatment | At Discharge

Case Report 2

A 82-years old male patient with impending ARDS presented to Sterling hospital Ahmedabad, India with an O_2 requirement of 15 liters/min. The patient contracted the H1N1 infection. He got post-aortic valve replacement. The patient received three successive 12-hour IV infusions of Aviptadil. Within 24 hours after the 1st dose of Aviptadil infusion, the oxygen requirement was reduced from 15 liters/min to 1 liter/min. The patient was stable at SpO2: 95% with supplemental oxygen FiO2: 55%. The patient was taken off supplemental oxygen therapy at the end of the Aviptadil 2nd dose infusion. After the 3rd infusion of aviptadil, the patient was discharged.



Before Treatment | After Treatment

Case Report 3
A 50-years old male patient with hypoxemia (SpO2 70%) presented with ARDS due to sepsis and associated multiple organ dysfunction syndrome at Bhimavaram Hospitals Limited, Bhimavaram, Andhra Pradesh, India. The subject was a known case of Type 2 Diabetes Mellitus. The PaO_2:FiO_2 ratio was 50 mmHg at the time of ICU admission. Aviptadil infusion was started for 3 consecutive days. It was observed that the requirement for oxygen and positive end-expiratory pressure (PEEP) decreased from 2nd dose onwards. At the end of the 3rd infusion, the PaO_2:FiO_2 ratio of the patient increased to 200 mmHg and he was discharged from ICU. PEEP improved from 15-20 cmH_2O to 5 cmH_2O.

Case Report 4
A 64-years old female patient with a past medical history of hypertension and hepatomegaly was admitted with moderate ARDS at Sunshine Global Hospital, Vadodara, Gujrat, India. She was maintaining 84% SpO2 on room air at the time of admission. The arterial gasometry showed hypoxia at 127 mmHg at the time of ICU admission. Aviptadil was administered for 3 consecutive days. After the Aviptadil treatment, the requirement for oxygen and positive end-expiratory pressure (PEEP) decreased and the PaO_2:FiO_2 ratio of the patient reached 200 mmHg within 3 days. The next day, she maintained an oxygen saturation of 94-97% on room air and the patient was discharged from the ICU.

Case Report 5
An 80-year-old female patient with moderate ARDS presented at Sunshine Global Hospital, Vadodara, Gujrat, India. At the time of presentation to the hospital, she had an oxygen saturation of 92% on room air. The patient had a past medical history of hypertension, diabetes mellitus and dyslipidemia. Aviptadil infusion was administered for 3 consecutive days. After the 3-day treatment with Aviptadil, the PaO_2:FiO_2 ratio improved to 282 mmHg. The patient was observed for the next 48 hours and discharged from the ICU.

DISCUSSION
ARDS is an inflammatory process which rapidly progresses to acute respiratory failure.[14] Clinically, the ratio between arterial partial pressure of oxygen (PaO2) and a fraction of inspired oxygen (FiO2), PaO2/FiO2, is currently used as a marker of ARDS severity. ARDS is defined by a known insult associated with hypoxia, bilateral radiographic pulmonary infiltrates, and a PaO2/FiO2 ratio <300 mmHg on PEEP of >5 cm H_2O as per berlin definition (2012).[15] In the presented case series, oxygen requirement in all the patients decreased and the oxygenation index improved to 200-300 mmHg within 3 days of initiating Aviptadil treatment.

The published case of ARDS was a pregnant patient in Houston Methodist Research Institute, Houston, USA, where rapid clinical improvement with PaO2/FiO2 ratio to 350 mmHg was seen from 123 mmHg showing the potential of Aviptadil treatment in treating respiratory distress.[16] In one more case of ARDS, PaO2/FiO2 ratio increased to 286 mmHg after 3 days of Aviptadil infusions from 146 mmHg.[17] In the same institute, eight other cases of ARDS associated with sepsis had PaO2/FiO2 ratio <100 mmHg, were treated with Aviptadil infusion and successfully removed from mechanical ventilation and discharged from intensive care.[18] Our case series confirms the similar potential of Aviptadil treatment in ARDS from varied etiologies.

VIP ameliorates cytokine storm and improves oxygenation in lung injury through its binding to the VPAC1 receptor of the Alveolar Type II cell. The role of type-II cells is to produce a surfactant layer and oxygen transfer, as well as to maintain the respiratory barrier.[19] Similar findings of cytokine storm were present in one of our presented cases and Aviptadil infusion reduced the severity and improved the patient's condition. In conclusion, the highly specific role of Aviptadil in the ARDS of varied etiologies may be vital in the improvement of pulmonary oxygenation. This series of presented cases may help as a lead for further clinical research to explore the treatment of ARDS with Aviptadil.

Conflicts of interest
There are no conflicts of interest.

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