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Recommended Citation

Siddiqui, S., Zubair, S., Khan, F. H. (2004). Case of inhaled prostaglandin E1 used to improve hypoxia in ARDS. *Journal of Pakistan Medical Association*, 54(12), 635-636.

Available at: https://ecommons.aku.edu/pakistan_fhs_mc_anaesth/191

Case Report

Case of Inhaled Prostaglandin E1 used to improve Hypoxia in ARDS

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Introduction

The 'adult respiratory distress syndrome', or ARDS, is a term used to describe the sudden onset of acute respiratory failure characterized by pulmonary edema arising from increased lung permeability.¹ By definition four essential components should be present: 1) chest X-ray evidence of bilateral infiltrates, 2) exclusion of heart failure, by a wedge of less than 20 mm HG or clinical examination, 3) underlying disease and 4) severe hypoxemia with a PaO₂ / FiO₂ ratio of < 200. ARDS is a physiologic syndrome, not a single disease which results in a ventilation- perfusion (v/q) mismatch within the lung due to areas of poor ventilation. As a result of the progressive hypoxemia, pulmonary vascular resistance also rises and can lead to right ventricular failure.^{1,2}

The clinical syndrome is a common pathway resulting from a wide variety of insults, which can be intra- or extra-pulmonary. Although it has been a well-known entity since the 'shock-lung' patients seen in the Vietnam war in 1967, the mortality still remains high.³ Many therapeutic modalities have been used, but no single treatment measure has shown significant improvement in mortality. These include recruitment maneuvers, prone positioning, high PEEP, low tidal volumes, inverse ratio ventilation and inhaled nitric oxide.⁴

In the last few years, prostaglandins have been experimentally used via inhalation, in order to improve perfusion selectively in the well ventilated areas of the lung. This reduces the V/Q mismatch and shunt, hereby improving oxygenation.⁵ Blood is thus diverted from areas of collapse to the well- ventilated ones. Studies suggest that in ARDS, inhalation of aerosolized PGE1 (a breakdown product of arachidonic acid with vasodilating properties) and nitric oxide (NO) in low concentrations equally improve pulmonary vascular resistance and gas exchange. NO is much more expensive and associated with several complications. PGE1 has also shown reduction in cytokine mediated alveolar cell injury. Previous studies indicated that PGE1 disaggregates platelets and reduces local vasoconstriction in the pulmonary circulation.⁶

Case Report

A 6 year old (FK), known case of acute lymphocytic leukemia (ALL) was admitted with cough for 1 week and shortness of breath for 1 day prior to presentation. Informed

Table. Arterial Blood gases before and after PGE1 nebulisation.

Day	Without PGE1	
Day 10		
Ventilator settings	AM Arterial blood gas	PM arterial blood gas
Pressure control 18	pH 7.31	pH 7.32
Respiratory Rate 35	PaCO ₂ 65	PCO ₂ 56
Peep 15	PaO ₂ 49	PaO ₂ 53
FiO ₂ 1.0	HCO ₃ 33	HCO ₃ 30
	Base excess 5	BE 3
	Saturation 79%	Saturation 84%
Day 11	First dose of PGE1	Three doses of PGE1
Ventilator setting	AM arterial blood gases	PM blood gases
Pressure control 16	pH 7.29	pH 7.22
Respiratory Rate 39	PaCO ₂ 53	PaCO ₂ 78
Peep 15	PaO ₂ 103	PaO ₂ 86
FiO ₂ 1.0	HCO ₃ 24	HCO ₃ 32
	BE -2	BE 3
	Saturation 96%	Saturation 93%
Day 12	5 doses of PGE1	8 doses of PGE1
Ventilator settings	AM arterial blood gases	PM arterial blood gases
PC 16	pH 7.30	pH 7.3
RR 39	PaCO ₂ 59	PaCO ₂ 67
Peep 15	PaO ₂ 61	PaO ₂ 56
FiO ₂ 1.0	HCO ₃ 32	HCO ₃ 35
	BE 5	BE 7.5
	Saturation 86%	Saturation 85%

consent was obtained from the family. He was admitted with a diagnosis of pneumonia based on chest X Ray findings and clinical picture. After two days he required intubation and ICU admission for progressive hypoxemia and bilateral diffuse infiltrates on CXR, in keeping with ARDS. He was sedated and relaxed for his worsening status requiring maximal ventilatory support. He was also started on clarithromycin, Septran and meropenem. On the fourth day, when despite a ventilatory support of 1.0 FiO₂ and pressure control ventilation with a peep of 15 cm H₂O, his PaO₂ did not improve more than 49 mmHg (Alveolar - arterial gradi-

arterial gradient of 450 mmHg), he was placed in a prone position⁷ for eight hours / day. He was also started on high dose IV methylprednisolone^{7,8} in accordance with management of ARDS, on day 6. However, his respiratory acidosis and hypoxia continued. His chest Xray continued to show a diffuse ground glass appearance.

On day 10, Alprostadil (PGE1)^{9,10} was nebulised over 30 minutes every six hours. The dose used was 5 mcgs. in normal saline. Over the next 12-24 hours a marked improvement in oxygenation was seen on his arterial blood gases (Table). His A-a gradient improved, however, his CXR remained unchanged. No other parameter (proning, ventilatory support, antibiotics) was changed during the therapy. This improvement in PaO₂ was not sustained and drifted down once again, despite increasing the PGE1 nebulisation frequency. He died on day 13 of admission following a bradycardic arrest and worsening sepsis.

Discussion

Alprostadil (PGE1) is a product of the arachidonic acid metabolism and causes vasodilation by increasing camp.¹¹ Intractable respiratory failure and hypoxemia leading to multi organ failure in ARDS patient remains a difficult to manage problem for most intensivists. It also presents a huge burden on health care costs. Although many strategies have been proposed and research is ongoing for finding remedies for this illness, no single therapy or maneuver has improved outcome or mortality. Inhaled vasodilators that affect the pulmonary vasculature selectively (i.e. only the perfusion of areas well ventilated) are appealing adjuncts in many cardiopulmonary conditions that require mechanical ventilation such as ARDS, COPD and Primary pulmonary hypertension.¹² Inhaled nitric oxide (NO) and aerosolized prostaglandins like PGE1 offer advantage of selective pulmonary vasodilation with minimal systemic effects.¹³ Both agents decrease peak airway

pressures (PAP), pulmonary vascular resistance (PVR) and in many cases improve oxygenation acutely; however, the effect has not led to improved long-term outcomes. Nitric oxide, besides being expensive and not readily available, has systemic side effects.^{14,15} Currently, their use remains investigational and no large randomised controlled trials have been done to see the efficacy.

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