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Case Report

Emergency use of nebulized milrinone, a phosphodiesterase 3 inhibitor, in status asthmaticus: a case report in Suriname

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Abstract: Data indicate the benefits of phosphodiesterase inhibitors as an add-on treatment in severe asthma, but mainly because of the limited tolerability, no compound reaches the market. Low- and middle-income countries (LMIC) face the challenge of successfully treating status asthmaticus, due to little or no access to expensive drug regimens. We describe a case of a 25-year-old man admitted to the ICU with status asthmaticus where nebulized milrinone was used as a last resort as there was no improvement with optimal standard management. After initiation of nebulized milrinone the patient could be smoothly weaned from ventilation and discharged.

Keywords: Asthma attack; PDE inhibitor; Milrinone; LMIC.

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1. Introduction

Asthma is a chronic disease of the airways for which the standard treatment consists of nebulization with bronchodilators and steroids [1]. While most cases can be controlled with standard treatment, 3-16% of hospitalized asthmatic patients deteriorate to a status asthmaticus resulting in respiratory failure. These patients require admission to the Intensive Care Unit (ICU) for ventilatory support. [2].

Milrinone, a phosphodiesterase inhibitor, can have therapeutic potential in asthma. They are however not widely used due to their side effects [3]. However, none of these drugs have made it to the market as an asthma treatment or have been considered an add-on treatment for a status asthmaticus [3]. Here, we present a case of an adult patient with status asthmaticus for whom nebulized milrinone, a PDE inhibitor, was used as a rescue drug.

2. Case Report

A 25-year-old male with a known history of severe asthma came to the Emergency Room (ER) in a status asthmaticus. He had extreme dyspnea and coughing and fever for two days already. On admission the temperature was 37.6 °C, he showed a tachycardia 145/min, tachypnea 38 breaths/min, saturation 90%, and inspiratory and expiratory wheezing. His first arterial blood gas in the ER was as follows: pH 7.106, $PaCO_2$ 46.3 mmHg, PO_2 69 mmHg, SaO_2 91.8%; BE 13.8 mmol/l, white blood cells count 10.0 × 109/L and C-reactive protein (CRP) 1.8 mg/L. The patient was transferred to the ICU.

He was intubated shortly after arrival due to respiratory arrest. Shortly after intubation paCo2 in the arterial blood gas was 178 mm/hg. He received nebulized salbutamol/ipratropium bromide and steroids, ketamine loading dose 2mg/kg and continued with 2.5mg/kg/hr., as well as 2-gram magnesium sulfate intravenously without any substantial effect. Treatment with vasopressors was required because of very low blood pressure.

Mechanical ventilation was nearly impossible, yielding a minute volume of maximally 1.6 liters, accompanied by persistent blocking of the ventilator.

The arterial blood gas after initiation of mechanical ventilation revealed the following values: pH 6.87, $PaCO_2$ 185 mmHg, PO_2 70.7 mmHg, and SaO_2 76.4%. As a last resort, one hour after admission, nebulization with milrinone 2 mg every half hour for 5 hours was administered. Within five to ten minutes, the minute volume of mechanical ventilation increased to 4 liters. Three hours after starting therapy with milrinone, the blood gas had improved to pH 7.19, $PaCO_2$ 45.9 mmHg, PO_2 322 mmHg and SaO_2 99.6%. After three days the patient was weaned from the ventilator and successfully extubated. A sari swab yielded a human bocavirus. He was discharged from the hospital after 9 days with salbutamol and beclomethasone inhalers.

3. Discussion

Treatment of status asthmaticus in refractory asthma presents a challenge to the physician and health services especially in LMIC where treatment options can be scarce. Our case suggests that in patients with status asthmaticus not responding to optimal standard intervention use of nebulized milrinone, a bipyridine compound that selectively inhibits PDE3 in low dosages, could be considered. Milrinone is generally used intravenously for cardiac support in patients with acute heart failure but also i.e., perioperative during cardiac surgery and for pulmonary hypertension. Increased pulmonary vascular resistance is also found in asthma exacerbation [4,5]. When nebulized, milrinone can directly improve vasodilation in the pulmonary circulation [6].

Anti-inflammatory effects of locally applied milrinone were also shown *in vitro* [7]. The vasodilation as well as the presumed anti-inflammatory properties of nebulized milrinone could thus have contributed to the improvement in our case. Furthermore, the short plasma half-life of 2 – 2.5 hours and the nebulized administration of milrinone might minimize the risks for side effects such as cardiac arrhythmias and hypotension [8,9]. Further studies are needed to validate the application of nebulized milrinone in patients with status asthmaticus.

4. Conclusion

Nebulized milrinone may represent a feasible treatment as an add-on therapy in the management of status asthmaticus refractory to standard management in mechanically ventilated patients.

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Supplementary Materials: None.

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