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Atracurium Infusion and Pulmonary Deterioration in Three Omani Infants

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Atracurium is used to relax skeletal muscle during controlled ventilation. We are presenting three cases of Omani infants, requiring mechanical ventilation, which developed pulmonary deterioration after starting them on atracuirum infusion. However, they responded well to discontinuing of the infusion. We concluded that atracurium infusion should be used judiciously in infants.

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Atracurium infusion has been used in infants to relax skeletal muscle during controlled ventilation. However, complications like progressive deterioration of the respiratory system compliance, acute bronchospasm, histamine release, paresis and myopathy have been associated with the use of these agents[1-7]. We are presenting three cases of Omani infants, which developed pulmonary deterioration after putting them on atraturium infusion. A literature review showed no such association reported earlier.

CASE 1

The patient was an eight-month old male Omani infant, a known case of broncho-pulmonary dysplasia (BPD), who got admitted to Paediatric Intensive Care Unit (PICU) for the management of respiratory failure. On admission chest x-ray showed signs of BPD with chronic lung changes. His admission blood gas showed respiratory acidosis (pH of 7.08 with pCO_2 of 16 kPa, pO_2 of 12.6 kPa, bicarbonate of 27 mmol/L and base excess of + 3.3 mmol/L). His complete blood count and blood chemistry were as follows: WBC of 11.6 x 10^9/L, hemoglobin of 10.7 g/dL and platelet of 106 x 10^9/L, Na^+ 135 mmol/L, K^+ 4.0 mmol/L, Urea 1.0 mmol/L, Creatinine 37 μmol/L, Glucose 7.1 mmol/L and Calcium 2.42 mmol/L. Infant was intubated and was put on intermittent mandatory ventilation (IMV) mode with the settings of : FiO_2 of 60%, peak inspiratory pressure (PIP) of 24 cm of H_2O, positive end expiratory pressure (PEEP)of 4 cm of H_2O and rate of 70/min. Atracurium infusion (0.3mg kg^{-1} hr^{-1}) was started as per unit protocol. Infant was also started on broad-spectrum antibiotics. For BPD he was started on diuretics and salbutamol infusion. Frequent suctioning and chest physiotherapy was done as per the unit protocol.

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The infant's condition deteriorated on ventilator in spite of continuing with the bronchodilator, diuretics and antibiotics. The chest x-ray taken 48 hours after the intubation and starting atracurium showed bilateral consolidation, possibly atelectasis, pneumonia or acute respiratory distress syndrome (ARDS). Ventilatory support was increased to keep up with the saturation (>90 %). Patient reached to a very high ventilatory setting with FiO_2 of 100%, rate of 100 /min and peak inspiratory pressure of 28 cm of H_2O. The blood gas showed a pH of 7.29 with PCO_2 of 7.4 kPa, PO_2 of 5.8 kPa, Bicarbonate of 23 mmol/L and base excess of -1. I mmol/L. To proceed with synchronised intermittent ventilation (SIMV) mode, decision was made to wean the patient from paralysis. Patient improved dramatically and got extubated as he was weaned from atracurium infusion. The bilateral white out of the lung fields was contributed to loss of compliance of the lungs secondary to atracurium, as Acute Respiratory Distress syndrome (ARDS) and pneumonia are less likely to respond so quickly. The repeat chest x-ray showed better aeration bilaterally.

CASE 2

The patient was a 5-month old Omani boy, with history of recurrent chest infections with inconclusive diagnosis of cystic fibrosis or immune deficiency. He got admitted to PICU for the management of increasing respiratory distress. The blood gas at admission, showed a pH of 7.38 with CO_2 of 7.1 kPa, PO_2 of 5.8 kPa, Bicarbonate of 30 mmol/L and base excess of + 6.7 mmol/L on FiO_2 of 50%. However, on examination patient was noted to be in severe respiratory distress with sub-costal retractions and tachypnea, necessitating intubation. Chest x-ray showed bilateral infiltrates.

The infant was put on IMV with the settings: FiO_2 of 50 %, PIP of 24 cm of H_2O**,** PEEP of 3 cm of H_2O and rate of 60/min. Patient was started on atracurium infusion (0.3mg kg^{-1} hr^{-1}) as per unit protocol. Complete cell count revealed WBC of 14.6 x 10^9/L, hemoglobin of 10g/dl and platelets of 460 x 10^9/L. Patient was started on broad spectrum antibiotics. For the chronic lung disease he was started on diuretic and salbutamol infusion. Frequent suctioning and chest physiotherapy was done as per the unit protocol. In spite of continuing with the broad-pectrum antibioitic, diuretic and bronchodilator therapy, the patients' condition continued to deteriorate. Chest x-ray taken four days after the therapy showed persistence of the infiltrate in the lung fields with more hazy appearance especially in the bases. To proceed with SIMV mode of ventilation, decision was made to wean the patient from paralysis. Patient started to improve as he was weaned from atracurium infusion and got extubated within 36 hr. The bilateral haziness on the bases of the lung fields was contributed to loss of compliance of the lungs secondary to atracurium, as ARDS and pneumonia are less likely to respond so quickly. The repeat chest x-ray showed better aeration bilaterally.

CASE 3

The patient was a 4-month old Omani girl, a known case of ventricular septal defect (VSD), with history of frequent chest infections. She was referred to PICU for further management of increasing respiratory distress. Her capillary blood gas at admission revealed severe respiratory acidosis (pH of 6.88 with PCO_2 of 17.5 kPa PO_2 of 6.3 kPa, bicarbonate of 15.8 mmol/L and base excess of -9.9 mmol/L). Chest x-ray showed a moderately big heart with bilateral infiltrates in the lung field. She was intubated and put on mechanical ventilation on IMV mode with PIP of 26 cm of H_2O, FiO_2 of 45%, PEEP of 4 cm of H_2O and rate of 40/min. Atracurium infusion (0.3mg $kg^{-1}hr^{-1}$) was started.

The infant was started on broad -spectrum antibiotics. Cardiology consultation was taken and diuretics and digoxin were added. Frequent suctioning and chest physiotherapy was done as per the unit protocol. Complete blood count revealed WBC of 13.3 x 10^9/L, hemoglobin of 9.3 g/dl and platelets of 384 x 10^9/L. Blood chemistry showed Na^+ 135 mmol/L, K^+ 4.4 mmol/L, urea 3.6 mmol/L, creatinine 43 μmol/L, glucose 14.9 mmol/L and calcium of 2.42 mmol/L.

No change in infant's condition was noted for four days. A repeat chest x-ray showed bilateral haziness . As we have seen two earlier cases like this, a decision was made to wean the infant from paralysis. Patient started to improve as she was weaned from atracurium infusion and got extubated within 24 hrs. The bilateral haziness of the lung fields was contributed to loss of compliance of the lungs secondary to atracurium, as ARDS and pneumonia are less likely to respond so quickly. The chest x-ray showed better aeration bilaterally.

DISCUSSION

An extensive Medline search revealed no such reports on atracurium infusion and pulmonary deterioration in infants. The exact mechanism by which atracurium caused the pulmonary deterioration in our cases is not clear. It may be due to damage caused by frequent pulmonary infections, compromising the normal architecture of the bronchopulmonary tree, thus making them sensitive to the use of pharmacological paralysis. In an interesting study, Schindler et al[1] have described the immediate and progressive deterioration of the respiratory system compliance caused by the skeletal muscle paralysis. In their study of fifty-three paediatric patients, they found that patient without paralysis had no changes in compliance as compared to patients with paralysis.

The other explanation for the pulmonary deterioration seen in our cases may be contributed to the association of acute bronchospasm, histamine release, paresis and myopathy, described with the use of atracurium in previous reports[2-7]. But our patients received appropriate bronchodilator therapy and none had signs of myopathy or paresis after extubation.

The element of chance occurrence cannot be fully eliminated in the cases, but in clinical setting, it will be difficult to establish a cause and effect relationship. The argument that the improvement noted in our cases after atracurium discontinuation might have just reflected the natural course of the disease, but such a fast and pronounced improvement, in all three cases, was against the natural history of chronic diseases.

Generally it is not considered to be a good practice to paralyse children in PICU unless extremely difficult to ventilate, as spontaneous movements and coughs provide good physiotherapy and prevent atelectasis. The alternative is the use of sedation (Benzodiazepine; Midazolam) and analgesic (Opioids; Fentanyl/morphine) without paralysing the children. Also patient triggered ventilation (PTV) mode, a promising mode of ventilation used in many institutions, may not be possible with the use of paralysis. In view of this and our experience with the described cases pharmacological paralysis, in an infusion form, should be used judiciously infants.

REFERENCES

1. Schindler MB, Bohn DJ, Bryan AC. The effect of single dose and continuous skeletal

paralysis on respiratory compliance in pediatric intensive care patients. Intensive Care Med 1996;22: 486-91

2. Doenicke A, Moss J, Lorenz W, et al. Are hypotension and rash after atracurium really caused by histamine release? Anesth Analg 1994;78:967-72

3. Naguib M, Samarkandi AH, Bakhamees HS, et al. Histamine release haemodynamics produced by rocuronium, vecuronium, mivacurium, atracurium and tubocurarine. Br J Anaesth 1995;75:588-92

4. Levitt RC, Ewart SL. Genetic susceptibility to atracurium-induced bronchoconstriction. Am J Respir Crit Care Med 1995;151:1537-42

5. Leatherman JW, Fluegel WL, David WS, et al. Muscle weakness in mechanically ventilated patients with severe asthma. Am J Respir Crit Care Med 1996;153:1686-90

6. Davis NA, Rodgers JE, Gonzalez ER, et al. Prolonged weakness after cisatracurium infusion: A case report. Crit Care.Med 1998;26:1290-2.

7. Tousignant CP, Bevan DR, Eisen AA, et al. Acute quadraparesis in an asthmatic treated with atracurium. Can J Anaesth 1995;42:224-7.