COLISTIN AND RESPIRATORY ACIDOSIS
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ABSTRACT
Antibioitic Colistin is used in many ICU to treat gram negative infection caused by multidrug resistant bacteria. However its use is associated with side effects prominent being neurotoxicity and nephrotoxicity. Here we report a case of severe respiratory acidosis leading to prolong ventilator support following use of intravenous Colistin.

Keywords: Intravenous Colistin, Respiratory Acidosis, Prolong Ventilator Support

INTRODUCTION
The increase prevalence of multidrug resistant organism in intensive care unit has given rise to use of potent modern broad spectrum antibiotics. However of late resistant to these antibiotics have also devoloped leading to reemergence of the use of colistin. Nephrotoxicity from colistin is well known, but its affect on respiratory system is seldom reported. Here I present a case of colistin induc ed respiratory failure leading to respiratory acidosis and prolong ventilator support which resolved once the drug was discontinued.

CASES
58 year old man was brought from another hospital on 22.4.2014 with history of bilateral pneumonia, sepsis, type 2 DM, hypertension of 10 days duration. During this period he was on mechanical ventilator and was tracheostomised and on central line. On arrival, he was conscious, oriented, afebrile, hemodynamically stable (Pulse-80/m, BP-130/70mmhg, Spo2-99%) on volume control ventilator support (TV-360, Fio2-50%, Peep-5cm water, RR-14breaths/min). Initial ABG revealed Po2-96mmhg, Pco2-44mmhg, PH-7.427, Hco3-24mmol. Hi blood parameters were-TC 6600 (N-60%, L-20%), HB-10.3gm/dl, S.CREATININE-0.6mg/dl, Platelet count-1.5lakh, CRP-36mg/dl. Blood sugar-130mg/dl. LFT-SGOT-24, SGPT-52, Total bilirubin-0.58mg/dl (D-0.2mg/dl,I-0.4mg/dl). Viral serology (A, E, B, C), PBS For mp, Leptospira serology were negative. Blood, urine, central line catheter tip culture were all negative on initial assessment. X-ray chest revealed consolidation in both lobes of lung with normal cardiac diameter. Echocardiography was normal and USG abdomen showed fatty liver change. Tracheal culture sent on 26.3.2014 showed moderate growth of klebsiella sensitive to imipenem, colistin, polymyxin-b. He was already on antibiotic imipenem (500mg iv 8hrly), forcan, tab telmisartan, and low molecular heparin (enoxaparin-40mg s/c od) from outside and based on the new tracheal culture report he was continued on same medication.

He was planned for early weaning and by 3rd day he was put on Simv (VC+PS) mode and then put on pressure support mode and he maintained normal ABG, good sensorium and hemdynamic stability. However on 30/3/2014 he became tachyneaic, with tachycardia, low spo2 (88%) on Simv (Vc+Ps). Clinically there was coarse creps on both lower lobes of lung with no raised JVP and third heart sound. ABG done revealed Po2-50mmhg, Pco2-36mmhg, PH-7.400, Hco3-21. D-dimer level was negative. X-ray chest showed infiltrates in lower lobes of lung. He was again put on volume control mode of ventilation. Tracheal culture showed profuse growth of pseudomonas sensitive to Colistin (MIC<=0.5), Levofloxacin (MIC<=1), Gentamcin (MIC<=1), Amikacin (MIC<=2), Cefepime (MIC 4), Cefoperazone (<=8), Ceftazidime (4), piperacillin (<=8). Resistant to imipenem and meropenum. Antibiotic was changed to Colistin (2miu Iv 8hrly) along with levofloxacin infusion (400 mg
iv OD). He was continued on this management for next 4 days following which there was improvement of his hemodynamic and arterial blood gas levels. Repeat tracheal culture sent on 3.4.2014 revealed again profuse growth of pseudomonas sensitive to Colistin (MIC\textless;=0.5), Levofloxacin (MIC\textless;=1), Gentamicin (MIC\textless;=1), pimeAmikacin (MIC\textless;=2), Cefepime(MIC 2), Cefoperazone (\textless;=8), Ceftazidime (2), piperacillin (\textless;=8), ticarcillin (16). Resistant to meropenum, imipenum, and tigecycline. Same antibiotic was continued and over next 2 days he was put on simv (Vc+PS) and then on intermittent pressure support ventilation.

X-ray chest done on 3.4.2014 showed resolving opacity of both lower lobes of lung with normal cardiac diameter On 9.4.2014 he was put on T-piece trial by after 2hrs he became tachypneic, with laboured breathing and after 4 hrs he became drowsy. ABG done revealed severe respiratory acidosis with PH-7.067, Po2-200.6mmhg, Pco2-135mmhg, Hco3-38.6.

Immediately put on full ventilator support. Total blood count, serum electrolytes, renal and liver function test, CRP were all within normal limits. Levofloxacin infusion was stopped in view of drowsiness. Next day he regained consciousness with ABG of PH-7.331, PCO2-70mmg, Pio2-104mmhg, Hco3-34.6. Again he was gradually weaned from ventilator keeping him on SIMV mode for 2 days and then intermittent Pressure support mode over next 2 days. On 13.4.2014 he was put on T-piece trial but after 4 hrs he again became drowsy and ABG done revealed respiratory acidosis-PH-7.21, Pco2-106mmhg, Po2-90mmhg and was again put on volume control mode. As his blood reports, CRP, LFT, RFT were all within normal range along with x-ray chest (resolving pneumonia) with no past history of asthma, COPD the possibility of colistin induced respiratory acidosis was thought in view he was receiving this antibiotic for last 15 days. Colistin was promptly stopped and substituted with cephalosporin group antibiotic.

Next day he was alert and put on T-piece trial for 2hrs and then on pressure support mode. This was continued next 3days and repeat ABG showed Po2-80mmhg, PCO2 of 56mmhg and PcaH-of 7.42. Clinically patient was alert, hemodynamically stable, with no tachpnea or laboured breathing. He was then kept on T-piece with close monitoring of his vitals and respiratory system and on day 22.4.2014 he was successfully extubated. He was kept in ICU for next 4 days where vigorous physiotherapy was done and was discharged on 27.4.2014.

DISCUSSION

The patient presented to us with bilateral pneumonia, with no history of asthma or COPD and intial ABG did not reveal respiratory acidosis. However after institution of intravenous Colistin to treat Pseudomonas infection he developed detoriation of respiratory parameters with respiratory acidosis culminating in difficulty in weaning and prolong ventilator support which successfully resolved quickly following its discontinuation. One could argue that the patient received an excessive dose of colistin. Product information (Colistineb®, Forest Laboratories, Kent, UK) recommends a dose of 1–2 MIU q8h in adults weighing more than 60 kg, which is, indeed, lower than the prescribed dose in our patient. However, in UK, a 7-year cohort study evaluating 258 patients of whom 86% were hospitalized in the ICU, colistin dose was standardized to 9 MIU/day.

No significant neurotoxicity was observed even when treatment was given for more than 4 weeks in this study Colistin is a polypeptide antibiotic composed mainly of poly¬myxin E1 and E2. It is administered parenterally as the prodrug colistimethate sodium, a fraction of which is hydrolyzed in vivo to colistin. Colistin causes rapid bacterial killing in a concentration-dependent manner. Following intravenous administration, the drug is mainly renally excreted, with 40% of the dose recovered in the urine within 8 hours. The side effects of colistic include parasthesia, renal impairment, vomiting, potentiation of neuromuscular blockade which are potentiated by aminoglycosides, muscle relaxant, steroids.

Diagnosis of neurotoxicity is mostly made on clinical grounds, making it difficult to dis¬criminate eventual colistin-induced neurotoxicity from the more frequently observed “critical illness polymyoneuropa¬thy” in ICU patients. In the critically ill patients receiving colistin, objective assessment is difficult, because many undergo mechanical ventilation and/or receive sedatives (Falagas et al., 2005).
Case Report

In most cases colistin induced neurotoxicity resolves on discontinuation of the drug though in severe cases may require hemodialysis.

Conclusion

As multidrug resistant strains begins to grow in many ICU necessating use of colistin, it is also important to monitor renal and respiratory parameters regularly so that its toxicity is detected early and treated promptly.

REFERENCES


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