INTRODUCTION
Due to high prevalence of respiratory illness in pediatrics especially in neonates and intensive, ventilatory support remains cornerstone of treatment. On prolonged ventilation, there is inflammation of lungs activated by oxygen toxicity, volutrauma, barotrauma and other injuries like infections. This inflammation causes capillary leak and fluid accumulation in lungs. There are few studies and case reports showing role of furosemide nebulization on patients of asthma, COPD, Dyspnea and neonates with BPD. We have tried furosemide nebulization on patients with ventilator and oxygen dependency which were difficult to wean.

METHODOLOGY
Total six patients were given trial with furosemide nebulization, out of them 4 were primarily admitted to our hospital in paediatric ICU, 2 of them were referred from adjoining hospital for weaning them from ventilator. Since there are lots of study on neonates with BPD we reviewed them and tried furosemide nebulization initially on chronically ill ventilator dependent patient. Dosage and frequency of nebulization- 3 mg/kg/dose of furosemide was used in frequency of 3 hourly in case of ventilator dependency and 6-8 hourly in case of oxygen dependency. Side effects like dyselectrolytemia, dehydration, increase in urine output and other adverse events were monitored.

Case 1- 3 year old female child, admitted initially at neurosurgery with complaints of fever for 1 month, right upper limb focal seizures and right hemiparesis for 10 days, MRI done revealed 7x7x7 cm tumor with perilesional edema and mass effect. Craniotomy done and tumor was excised, histopathology examination diagnosed PNET (primitive neuroectodermal tumor). Child was taken to PICU postoperative on ventilator with settings of PIP -14, PEEP- 5, Rate- 25, Fio2- 40%. At the site of craniotomy child developed subgaleal abscess, patient was running high grade fever continuous, on day five child developed shock which responded on upgrading antibiotics. On day 11 of ICU child was given extubation trial but failed, ventilation was resumed with same settings. On day 22 fio2 increased to 55%, chest xray was done showed bilateral opacities, ventilation continued settings decreased gradually, multiple failed T piece trials were given. On Day 30, tracheostomy was done and ventilation continued with minimal settings of PIP- 12, R- 10, PEEP- 5%, fio2- 40%. On these settings several T piece trials were given but failed. On repeating chest x ray clearing was seen. Repeat CT chest done keeping possibility of metastasis was found normal. Total duration on ventilator was 40 days. Child was given furosemide nebulization consent for which was taken from parents, after 24 hours of nebulization child was taken on T piece with oxygen, in next 24 hours child was taken off oxygen and shifted out of PICU.

Chemotherapy started on patient, however due to toxicity secondary to chemotherapy child developed icterus, developed acute hepatic failure and died after 2 weeks of starting chemotherapy.

Case 2 - Our second case was a 1 year old female child admitted initially at some other hospital with complaints of Fever, Loose stools and Vomiting for 3 days, child had severe dehydration and shock, developed irritability and seizure, child had deranged KFTs and peritoneal dialysis was done. On day 7 of illness repeat seizures...
was present, MRI done showed findings suggestive of PRES for which child referred to us. On arrival child was gasping, cyanosis was present, immediately child was taken on ventilator with settings of PIP-18, PEEP – 5, R – 20, Fio2- 50%. Renal function was found to be deranged peritoneal dialysis was continued. On day 10 T-piece trial was given but failed. Fever was persisting, child developed sepsis, blood culture shown klebsiella antibiotics upgraded as per sensitivity, chest x-ray – bilateral opacities were present, ventilation continued, on day 23 of illness child self extubated herself but was not able to maintain saturation and developed respiratory distress. On day 27 – tracheostomy was done and ventilation continued with minimal settings of PIP-12, PEEP- 5, Fio2 – 40%. Rate-25. Multiple T piece trials were given but failed. Child was given furosemide nebulization, after 12 hours of nebulization child was taken on T piece and off oxygen after 48 hours of nebulization. Child was discharged, on follow up tracheostomy site was closed, child found healthy and asymptomatic on follow-up.

Case 3: Our third case was 75 days old male child delivered at 30 weeks gestation with birth weight of 1600gm. He was admitted in nursery for respiratory distress and kept on oxygen and given IVF for 7 days. He was started on RTF and discharged, however parents complaining of fast breathing since date of discharge. On day 5 of discharge and day 18 of life child had worsened respiratory distress, child readmitted at some other hospital and given oxygen. At day 45 of life child had apnea for which child ventilated (7 days) child kept on oxygen given off oxygen trials but failed for which child transferred to us. On transfer child had good activity, respiratory rate were 46 per minute and was orally accepting well. On giving of oxygen trial child desaturate and develop bradycardia. On investigating HB- 13, Sepsis screen –ve, ionized calcium level was normal, USG cranium done was normal and CSF done revealed normal values. Baby nebulized with furosemide after 48 hours of nebulization child was taken off oxygen, on follow up no respiratory distress, no apneas noted and found thriving well.

Case 4: Child admitted with complaints of fever, cough for 8 days and respiratory distress for last 3 days. On examination respiratory rate was 60 per minute, retractions were present and bilateral wheeze and crept were auscultated in chest. Chest x-ray was done showed bilateral nonhomogeneous opacities. Child nebulized with asthalin, oxygen given by mask and antibiotics continued. Respiratory distress was worsened in between which required magnesium sulphate infusion. Five weeks passed, despite of upgrading higher antibiotics, respiratory distress was persisting and oxygen requirement had increased. Bronchoscopy done was normal, CECT chest revealed consolidation in right upper and lower lung and in left lower lung. We had given him furosemide nebulization trial, 48 hours later respiratory distress improved, over next 48 hours oxygen was removed. Child was discharged and is healthy on follow-up.

Case 5: Our fifth case was a 5 month old male child admitted in adjoining hospital where child was diagnosed truncus arteriosus type 1, repair was done of pulmonary artery with pericardial conduit from RV-PA. Child ventilated post-operative given CPAP trial but was not able to wean, tracheostomy was done. After 4 weeks of ventilation child referred to us. Initial settings on which we started ventilation was PIP – 12, PEEP- 5, Rate- 25, Fio2- 45%. Child given CPAP trial but failed and taken back on ventilator, total duration of ventilation was 8 weeks, multiple attempts were made to wean off patient but failed, we have given him furosemide nebulization, 24 hours later child was taken on T piece and within next 24 hours child was off oxygen. On follow-up tracheostomy site was closed and child found asymptomatic.

Case 6: Our sixth case was 6 months old male child admitted in adjoining hospital with diagnosis of Obstructive TAPVC with nonrestrictive ASD with PFO with Severe PAH, TAPVC repair was done with ASD closure, PFO kept open. Child taken on ventilator post operatively, settings PIP- 18, rate- 35, PEEP- 5, Fio2 – 60%. Child referred to us for weaning. Initial settings kept were – PIP – 20, PEEP – 5, Rate -40, Fio2- 45%. Ventilator weaning tried; settings brought down to PIP – 16, PEEP – 5, Rate- 20, Fio2 – 40%. T- Piece trial was given but failed. We have not done tracheostomy in this patient, we started him on furosemide nebulization earlier in this patient 36 hours later child extubated successfully, taken off oxygen in next 48 hours and discharged.

RESULT SUMMARIZED
All six patients who were ventilator and or oxygen dependent after nebulization with furosemide were weaned off ventilator within 24 to 48 hours of nebulization and off oxygen within 48 hours of furosemide nebulization. All patients were discharged except one who died 2 weeks later of unrelated complication secondary to chemotherapy. Two patients out of six were referred from other hospital postsurgical for ventilator dependency and were successfully taken off ventilator and discharged.

No side effects were observed, no evidence of dehydration and dyselectrolytemia were observed in any patient. Mild increase in urine output was noted in 3 patients when started nebulization which does not appears significant, no weight loss and signs of dehydration were noted.

DISCUSSION
Administration of drug directly into lungs has been used since 1950s.[1] Delivering drug into lung is useful in intensive care settings where prompt response is needed. Ventilatory support is mainstay of treatment due to high
prevalence of respiratory disease in pediatrics especially neonate and intensive care. On prolonged ventilation, inflammation of lung is activated by oxygen toxicity, barotrauma/volutrauma or other injury like infection. The inflammatory process causes capillary leak and fluid accumulation in lung.[2]

Furosemide nebulization has been used in various trials on neonates with bronchopulmonary dysplasia (BPD) since systemic use of furosemide results in significant side effects. Five studies have been assessed for furosemide nebulization on total 57 infants with BPD, with dose of 1mg/kg/dose except for one study all 4 shows significant improvement in pulmonary function without any side effects.[3] In BPD patients furosemide nebulization appears to reduce interstitial lung water, improve gas exchange, decreases pulmonary vascular resistance and decreases oxygen requirement.

Few studies have been done on asthma patients, nebulization with furosemide has improved spirometric values significantly in asthmatic patients however dose used was low.[4,5,6] A randomized control trial was done among infants with bronchiolitis who received 2mg/kg/dose of furosemide nebulization in a group of 16, had significant reduction in oxygen requirement post thirty minutes inhalation.[7]

Proposed mechanism of action includes:
A) Na/K/Cl channel inhibition in pulmonary airway epithelium causing changes in osmolarity and fluid clearing.[8,9]
B) Inhibition of release of LTC4, histamine, neutrophil chemotactic factor, causing decreased inflammation.[10]
C) Reduction in intracellular Na and Ca causing smooth muscle relaxation.[9]
D) Increase in epithelial PGE2 and PGI2 both are vasoprotective.[11]

All of the studies done were limited to few patients only, large data has to be studied, randomized control trials needed to prove the role of furosemide nebulization.

CONCLUSION
We have tried furosemide nebulization among patient with ventilator and oxygen dependency though number of patients was very low however, we found very amazing results in all patients. Trials with large sample size needed to further prove its efficacy.

REFERENCES