Role of Steroid (Dexamethasone) in Meconium Aspiration Syndrome

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LIST OF ABBREVIATIONS

AGA	-	Appropriate for Gestational Age
AP 1	-	Protein Activator 1
B/N Ratio	-	Band Neutrophil Ratio
COX- 2	-	Cyclooxygenase- 2
CFT	-	Capillary Filling Time
CRP	-	C - Reactive Protein
DBF	-	Direct Breast Feeding
ECMO	-	Extracorporeal Membrane Oxygenation
ET-1	-	Endothelin-1
GA	-	Gestational Age
HC	-	Head Circumference
HIE	-	Hypoxic Ischemic Encephalopathy
HFV	-	High Frequency Ventilation
ICAM-1	-	Intercellular Adhesion Molecule 1
IL-1	-	Interlukin- 1
IL-6	-	Interlukin- 6
IL-8	-	Interlukin- 8
iNO	-	Inhaled Nitric Oxide
IPPV	-	Intermittent Positive Pressure Ventilation
LSCS	-	Lower Segment Caesarean Section
MAS	-	Meconium Aspiration Syndrome
MSAF	-	Meconium Stained Amniotic Fluid
NF-κB	-	Nuclear Factor - κB
NICU	-	Neonatal Intensive Care Unit
NVD	-	Normal Vaginal Delivery
PAF	-	Platelet Activating Factor
PEEP	-	Positive End Expiratory Pressure
PLA2	-	Phospholipase A2
PPHN	-	Persistent Pulmonary Hypertension
RBS	-	Random Blood Sugar
SD	-	Standard Deviation
SGA	-	Small for Gestational Age
TLC	-	Total Leucocyte Count
TNFα	-	Tumor Necrosis Factor α

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INTRODUCTION

Meconium aspiration syndrome (MAS) is an important cause of respiratory distress in term newborn babies. The overall frequency of MAS varies between 5-25% (median 14%) MAS occurs in around 10% of babies born through meconium stained amniotic fluid (MSAF)[1].

The most important consequence of neonate born through meconium stained liquor is meconium aspiration syndrome (MAS). It is one of the major cause of severe respiratory distress in newborn[2].

The pathophysiology of MAS is not completely understood. Meconium aspiration leads to activation of pulmonary macrophages producing an intense inflammatory response and infiltrations of polymorphonuclear lymphocytes diffusely through the lungs[3].

There is associated increased pulmonary vascular permeability, leading to proteinaceous exudation into the alveolar spaces and thereby causing inactivation of pulmonary surfactant and decreased lung compliance.

Since inflammation plays an important role in the pathophysiology of MAS, suppression of inflammation by corticosteroids appears to be of potential benefit. The synthetic glucocorticoid (dexamethasone) have metabolic and anti - inflammatory effects, their anti-inflammatory action results from inhibition of transcription factors including nuclear factor (NF)-κB and protein activator (AP)-1 inhibits the expression of pro-inflammatory cytokines (IL-1, IL-6, IL-8, TNF-α, etc.), enzymes (PLA2,COX-2, iNOS, etc.) and other biologically active substances such as PAF, ET-1, ICAM-1, etc[4].

By stabilizing the cell membranes and decreasing the production of proinflammatory and vasoactive substances, glucocorticoid reduces microvascular permeability. In addition, by direct modulation of the pulmonary vasomotoric tone, glucocorticoid diminishes pulmonary vasoconstriction and inhibits fibrogenesis[5].

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LITERATURE REVIEW

Definition:

Meconium aspiration syndrome (MAS) is defined as ―respiratory distress in newborn infants born through meconium-stained amniotic fluid (MSAF) whose symptoms cannot otherwise be explained [6].

Epidemiology

In Europe the incidence is between 1:1000 and 1:5000, whereas in North America rates of 2-5: 1000 have been reported[7]. In Australia and New Zealand, the rate of MAS was 0.43:1000, with a decrease in incidence between 1995 and 2002 (Dargaville and Copnell 2006). However in developing countries, the incidence is considerably higher[8].

The overall frequency of MAS varies between 5-25% (median 14%). It occurs in around 10% of babies born through MSAF[1]. Most babies with MSAF are 37 weeks or older and many are postmature (>42 weeks).

Etiology

Meconium aspiration was intially considered to be a postnatal event caused by aspiration of meconium at the first breath[9]. Suctioning of trachea and oropharynx at delivery decreased the incidence of mild and moderate MAS[10].

It is no longer considered to be a postnatal disorder caused by postnatal aspiration, but rather a disorder with antepartum, intrapartum and neonatal cause[11]. Meconium aspiration may occur in utero, during or after delivery. Chronic in utero insult may be responsible for severe MAS[12].

Vain et al showed that routine intrapartum oropharyngeal and nasopharyngeal suctioning of term gestation infants born through MSAF did not prevent MAS[13]. Ghidini et al reviewed the literature and concluded that severe MAS is caused by chronic asphyxia or intrauterine infection[14].

Meconium has been found in the lungs of stillborn infants and infants who died soon after birth without a history of aspiration at delivery[15].

Risk factors

Signs of fetal compromise like abnormal fetal heart rate and/or low Apgar scores increase the risk of MASF leading to MAS[16].

There is an increased risk of MAS in Africans17 and in Afro Americans compared to other Americans. Advanced gestation is a risk factor of both MASF and MAS[18].

Risk factors for developing respiratory distress in infants born through meconium-stained amniotic fluid are male gender, abnormal biophysical profile,

abnormal fetal heart rate, low Apgar score, oligohydramnios, caesarean section, preeclampsia or eclampsia and maternal diabetes mellitus[19].

Pathophysiology

MAS has a complex not well defined pathophysiology[6]. Several factors are involved including -

1. Direct toxicity of meconium and its constituents resulting in alveolar and parenchymal inflammation with release of inflammatory mediators, edema and protein leakage into the alveoli, tissue necrosis and apoptosis in the lung and ulcerations of the umbilical cord.

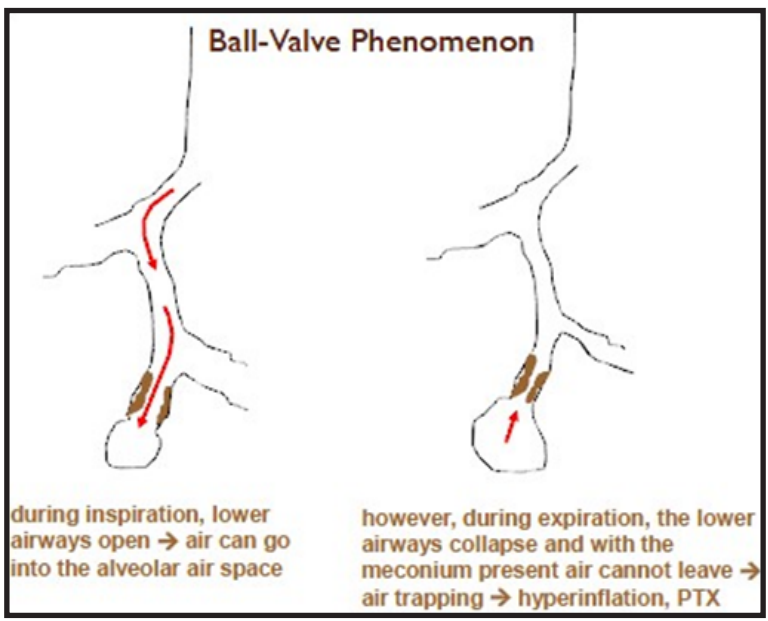
2. Airway obstruction caused by meconium, edema fluid, protein exudates and blood cells.

3. Altered elastic forces in the lungs resulting in increased resistance and decreased compliance.

4. Inactivation and dysfunction of surfactant caused by meconium, protein and inflammatory cells leading to atelectases, air trapping, pneumothorax, right to left shunting,

5. In utero hypoxemia leading to pulmonary vascular remodelling and lung parenchymal changes, and vasoconstriction of placental and umbilical vessels.

6. Ventilation perfusion mismatch contribute further to acidosis, hypercapnia and hypoxemia.



Picture 1: Ball – valve phenomenon

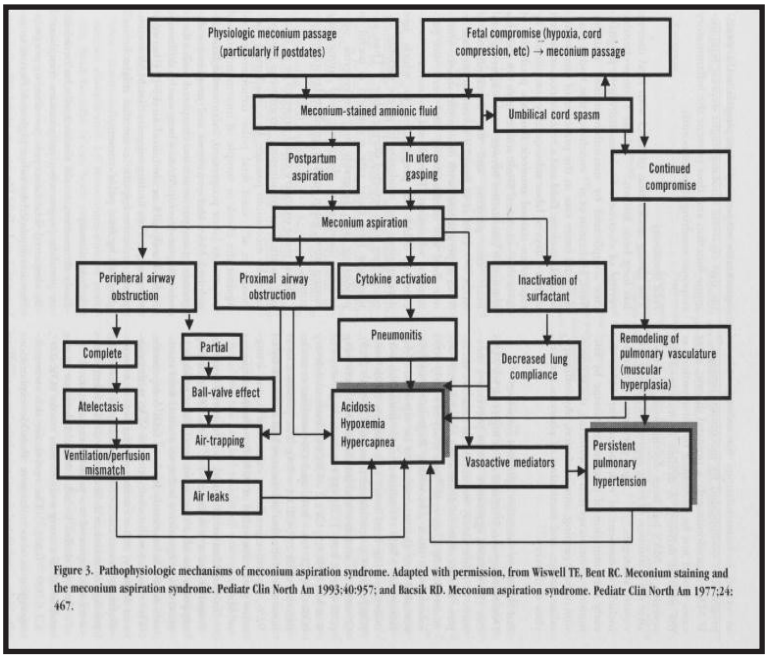


Figure 3. Pathophysiologic mechanisms of meconium aspiration syndrome. Adapted with permission, from Wiswell TE, Bent RC. Meconium staining and the meconium aspiration syndrome. Pediatr Clin North Am 1993;40:957; and Bacsik RD. Meconium aspiration syndrome. Pediatr Clin North Am 1977;24: 467.

Picture 2: Pathophysiologic mechanism of meconium aspiration syndrome

MSAF is rarely detected before 37 weeks of gestation[20], but occurs in more than one third of pregnancies lasting longer than 42 weeks[18]. Prenatal passage of meconium is normally prevented by lack of intestinal peristalsis caused by low motilin levels, tonic contraction of the anal sphincter[21].

The incidence of clinical chorioamnionitis is significantly higher in the presence of MAS[22]. Among women in preterm labor, the prevalence of positive amniotic fluid cultures after amniocentesis is significantly higher in those with MASF as compared to those with clear fluid[23].

Histological evidence of acute placental inflammation is present in majority of cases of severe MAS[24], supporting the fact that intrauterine infections may contribute to a proportion of cases of severe MAS. This is supported by the lack of studies that directly correlate the severity of MAS with the amount of meconium aspirated, the thickness of meconium and the duration of exposure to meconium[25].

Incidence of severe MAS is higher in post-term infants[26]. Placental ischemic changes suggesting long compromise of utero-placental bloodflow[27] leading to pulmonary vascular hypertrophy is found in almost all cases of severe MAS also may be found in the absence of meconium passage and chronic in utero hypoxia may lead to persistent pulmonary hypertension of the newborns (PPHN)[28].

Meconium:
Meconium is blackish-green, odourless and varies in amount from 60 to 200g[29]. Meconium consists of 72-80% water[15].

It is a sterile, thick, black-green, odourless and contains secretions from salivary and intestinal glands like mucus, bile and bile acids, fatty acids and steroids from the gut, cellular debris, lanugo hair, components of vernix caseosa, amniotic fluid and blood group specific glycoproteins, drug metabolites[30].

It may also contain various amounts of proinflammatory substances including TNF-α, IL-1, IL-6 and especially IL-8[31].

Description of meconium[15]:
1. Watery: Amniotic fluid that is thinly stained.
2. Moderately stained fluid: Opaque without particles.
3. Pea soup: Fluid with thick meconium with particles.

Effect of meconium on the lungs and vessels:
Respiratory symptoms may be secondary to meconium aspiration in utero or at birth, or to alterations in the pulmonary vasculature secondary to asphyxia or to meconium itself[32]. MAS is believed to be caused by a combination of mechanical blockage of the small airways and chemical pneumonitis induced by meconium particles aspirated[28].

Aspiration of meconium may cause partial obstruction of the airways with air trapping and atelectasis and development of air leaks or complete obstruction with alveolar collapse and ventilation-perfusion mismatch[33]. Estimated risk of pneumothorax is 15-33%[6].

Mechanical dysfunction of lungs is more severe during the early phase of MAS with lower dynamic and specific lung compliance and increased airway resistance[34]. Vasospasms, hypertrophy of the pulmonary musculature, and pulmonary hypertension lead to right to left shunting through the foramen ovale and ductus arteriosus. It is the most common cause of PPHN[35,36], with abnormally constricted pulmonary vasculature.

Meconium injury triggers postnatal release of vasoactive mediators like endothelin-1, thromboxane-A2 and prostaglandin E2[37, 38]. Meconium induced a dose- dependent oxidative burst in neutrophils with increased levels of vasoactive peptides[39].

Surfactant displacement and inactivation:
Meconium, protein and inflammatory cells inactivate surfactant function and alter surfactant production[40]. Meconium displaces surfactant from the alveolar surface and inhibits surfactant function reducing its ability to reduce the surface tension.

In high enough concentrations, meconium has a direct cytotoxic effect on type II pneumocytes[41]. Bronchial lavage fluid from infants with MAS contained increased levels of albumin, total protein and membrane-derived phospholipids compared to controls. The inhibition of surfactant in the alveolar spaces may be mediated by meconium, plasma proteins, edema fluid and hemoglobin.

Meconium aspiration syndrome and inflammation:

Toxic effects of meconium trigger inflammation in the lungs[42]. Activated neutrophils and macrophages are detected in the lung parenchyma and alveoli only hours after meconium aspiration[43].

Meconium activates the complement system both in vitro[44] and in vivo in an experimental model of MAS in newborn pigs[45] which is associated with release of proinflammatory cytokines. The proinflammatory cytokines may directly injure the lung parenchyma resulting in vascular leakage causing pneumonitis and pulmonary edema[46]. Most proinflammatory cytokines and chemokines measured, as well as the anti-inflammatory cytokine IL-10, were significantly elevated in sera from neonates with MAS[47].

Meconium-induced inflammatory lung injury is associated with respiratory epithelial apoptosis in several animal models[48]. Meconium activates the pulmonary renin angiotensin system shown by an increase in angiotensinogen m-RNA associated with apoptosis and cytokine release. Angiotensin-II receptor, which is expressed in several cell types in the newborn lung, including bronchial and alveolar epithelium and bronchial and vascular smooth muscles are up-regulated after meconium exposure[49].

Prenatal management:

Transcervical intrapartum infusion of saline into the amniotic cavity has been proposed to reduce the risk for MAS. An inverse relationship has been found between amniotic fluid volume and fetal heart rate decelerations. The proposed mechanism is mechanical cushioning of the umbilical cord to prevent recurrent umbilical compressions leading to fetal acidosis and dilution of meconium to reduce mechanical and inflammatory effects[50].

A systematic review of the literature by Xu concluded that only in settings with limited peripartum surveillance and where complications are common, amnioinfusion appeared to reduce the risk of MAS[50]. There are adverse outcomes of amnioinfusion, which include increased incidence of cord prolapse, infection and requirement of instrumental delivery.

Delivery room management:

Thorough oropharyngeal suctioning before delivery of the infants shoulders has long played an important role in preventing MAS. This approach has been recently challenged because despite effective suctioning at birth some babies develop MAS due to aspiration of meconium in- utero. Carson et al demonstrated

in 1976, a decreased incidence of MAS after intrapartum oropharyngeal suctioning[51].

Vain et al showed that routine intrapartum oropharyngeal and nasopharyngeal suctioning of term-gestation infants born through MSAF did not prevent MAS[52].

Rossi and colleagues recently reported oropharyngeal suctioning to result in higher 1 and 5 minute Apgar scores and less need for mechanical ventilation[53].

Still the American Academy of Pediatrics and American Heart Association recommends intubation of all infants born through moderately thick or thick consistency MSAF.

Clinical features:
Infants with meconium aspiration are often postmature and have visible meconium staining of the nails, skin and the umbilical cord. Thick pea soup consistency of MSAF is mostly associated with MAS compared to thin consistency[6].

Respiratory:
Infants with MAS typically have respiratory distress with marked tachypnoea, use of accessory muscles as evidence by intercostals and subcostal recession, flaring of nostrils and an expiratory grunt may be heard. It can cause air trapping and an overdistended chest with an increased anteroposterior diameter. Baby may remain symptomatic for only 24 hrs or may be dyspnoeic for 7 – 10 days before recovery[7].

Evaluation of Respiratory Distress Using Downes' Score

	0	1	2
Respiratory Rate	< 60/min	60 – 80/min	> 80/min
Retractions	No retraction	Mild retractions	Severe retractions
Cyanosis	No cyanosis	Cyanosis relieved by O_2	Cyanosis on O_2
Air Entry	Good bilateral air entry	Mild decrease in air entry	No air entry
Grunting	No grunting	Audible by stethoscope	Audible with ear

Score < 4 — No / mild respiratory distress
Score 4 -7 — Respiratory distress
Score > 7 — Impending respiratory failure

Picture 3: Downe's score

Cardiovascular

In the absence of asphyxia damage to the myocardium, there are no specific cardiovascular features of MAS. If PPHN develops, S_2 may remain single, and there may be murmur of tricuspid incompetence[7].

Gastrointestinal system

Liver and spleen are palpable if there is downward displacement of the diaphragm caused by air trapping. In a severely affected infant, bowel sound may be absent, with delayed passage of meconium[7].

Central nervous system

Depending on the severity of coexisting neurological insult, the baby can be neurologically normal or may show features of birth depression (HIE). Convulsion may occur[7].

Treatment: Prevention of MAS

The decrease in the incidence of MAS in the last decade is due to the reduction in postterm delivery, aggressive management of abnormal heart rate monitoring and decreased number of infants with low Apgar score.

It is important to observe and monitor all infants born through MSAF for hypoxia or respiratory distress for at least 6 hours. There is no specific treatment for MAS.

Management is primarily supportive. Maintenance of optimal thermal environment and minimal handling is essential because these infants are agitated easily, which causes right to left shunting leading to hypoxia and acidosis.

Maintenance of adequate oxygenation, correction of hypoglycaemia, acidosis and other metabolic disorders is the mainstay of treatment.

Role of Antibiotics

The presence of meconium increases the chances of positive cultures from amniotic fluid in preterm and term infants. However, studies evaluating the development of sepsis in infants with MSAF failed to demonstrate that relationship[54].

Three randomized control studies reported that routine antibiotic prophylaxis is not recommended in the management of MAS for those without perinatal risk factors[55]. The role of antibiotics in the management of MAS may need to be re-evaluated in well designed trials. Unless there is definite risk for infection, prophylactic use of antibiotics in MAS did not reduce infection. If antibiotics are started for suspected infection due to perinatal risk factors, discontinuing antibiotics once the blood culture results are negative is being considered.

Ventilation

Ventilator management of the neonate with MAS is challenging because of the complicated pulmonary pathophysiology resulting from areas of atelectasis and

areas of hyperinflation, in association with ventilation perfusion mismatch and airway compromise[56].

Approximately 40% of babies with MAS require mechanical ventilation and additional 10% require continuous positive airway pressure[57].Ventilation should be aimed at increasing oxygenation while minimizing the barotrauma that lead to air leak syndromes.

The amount of ventilator support depends on severity of respiratory distress. Some infants only require oxygen by hood. In infants with MAS without PPHN, it is sufficient to maintain a pH of 7.3–7.4, with PaO_2 targeted between 60 and 80mmHg and $PaCO_2$ of 40–50mmHg. Infants may be started with a moderate peak inspiratory pressure (PIP) preferably not exceeding 25cm H_2O, a relatively rapid ventilator rate (40–60/min), a moderate positive end expiratory pressure (4–6 cm H_2O), and an adequate expiratory time (0.5–0.7 sec) to prevent gas trapping and air leaks.

If gas trapping is noticed, expiratory time may be increased and PEEP should be decreased (3-4 cm H_2O)[56,57]. In infants with MAS and concomitant PPHN, mild hyperventilation and higher FiO_2 can be considered. But the strategy of achieving hypocapnia and alkalosis by hyperventilation has adverse effects including cerebral vasoconstriction leading to long-term neurologic morbidity as well as air leaks[58]. In such situations other modalities like inhaled nitric oxide and high frequency ventilation should be considered early.

Theoretically High Frequency Ventilation (HFV) minimizes the barotrauma and reduce air leak syndrome in MAS. No prospective randomized trials have compared conventional ventilation versus HFV in MAS.

In pilot studies using inhaled nitric oxide (iNO), Kinsella and Abman found that the combination of HFV and iNO causes greatest improvement in oxygenation in some patients with severe PPHN[59].

Partial liquid ventilation was found to be a better method of delivering surfactant in an adult rat model of MAS when compared with conventional mechanical ventilation[60]. There is no randomized clinical trial about the use of partial liquid ventilation in neonates with MAS.

Surfactant Therapy

In vitro studies have shown that meconium interferes with surfactant in several ways[6]:

1. Inactivation of its function depending on the concentration
2. Direct toxicity on type II pneumocytes
3. Displacement of surfactant from the alveolar surface
4. Decrease of surfactant protein A and B levels.

Canadian Pediatric Society position statement recommends that intubated infants with MAS requiring more than 50% oxygen should receive exogenous surfactant therapy[61].

Meta-analysis of 4 RCTs showed reduction in the severity of respiratory illness and decrease in the number of infants with progressive respiratory failure requiring ECMO. However, there was no significant difference in mortality, hospital stay, length of ventilation, duration of oxygen use, pneumothorax, pulmonary interstitial emphysema, or chronic lung disease. Dargaville and colleagues reported that lung lavage with dilute surfactant (Survanta) in ventilated infants with severe MAS does not decrease the duration of respiratory support, but may produce a reduction in mortality[62].

Role of Steroids

In 2003, Cochrane meta-analysis of two trials[63] including 85 infants with MAS showed that there was no difference in mortality but a small increase in the duration of oxygen treatment in steroid treated group[5].

Since then, two more trials reported that steroid therapy in MAS was associated with a decrease in the duration of oxygen therapy and hospital stay[2,64]. The choice of steroid and duration of therapy was different between the studies.

Steroids may be beneficial in severe MAS with apparent lung edema, pulmonary vasoconstriction, and inflammation. At present, there is no conclusive evidence to propose routine steroid therapy in the management of MAS.

Further research is needed regarding the dosing, timing and ways of administration of steroids considering their individual properties and possible acute and long term side effects[4].

Nitric Oxide:

Severe MAS is often associated with PPHN, resulting in severe hypoxemia. Randomized clinical trials have demonstrated that iNO therapy decreases the need for ECMO in addition to mortality in full-term and near-term neonates with hypoxic respiratory failure and PPHN[65]. For hypoxic respiratory failure due to MAS, infants responded well to combined iNO and HFV as compared to either treatment alone[66].

Extracorporeal Membrane Oxygenation:

ECMO has been used as a final rescue therapy in infants with severe and refractory hypoxemia associated with MAS. Use of ECMO has been decreased significantly in developed countries with the availability of iNO and HFV. Infants with MAS make up approximately 35% of the infant population who require ECMO[67]. The survival rate has approached 95% of infants with MAS who underwent ECMO[68]. In the ECMO registry, the highest survival rates (>90%) were seen in the patients with MAS who qualified for ECMO[69].

Complications:
Despite advances in the understanding of pathophysiologic mechanisms of MAS and therapeutic advances in the management of respiratory failure and PPHN in newborn babies outcome of MAS is guarded[70].

The case fatality rate vary between 5 and 35 %[70]. The majority of deaths are from respiratory failure, PPHN and airleaks.

There is high risk of cerebral palsy, seizures and mental retardation depending on the severity and duration of perinatal hypoxia.

Pneumothorax, air leaks
Pneumothorax, pneumomediastinum, pneumopericardium and pneumoperitoneum can all occur. Approximately 50% of ventilated MAS babies suffer some from air leak.[7]

Persistent pulmonary hypertension (PPHN)
It is a common complication of severe MAS and appears to be a frequent fatal case[7]

Bronchopulmonary dysplasia
This is a rare complication of MAS, although it may occur in any baby who survives after long term high pressure IPPV.

Related studies
In a study by Garg N et al, the role of early inhaled budesonide therapy in meconium aspiration syndrome, a randomized control study in 2016, a total of 78 neonates were included in the study. After randomization, intervention group received nebulization with budesonide (0.5 mg dissolved in 2.5ml sterile normal saline within 2 hours of birth and second dose was given at 12 hours of birth) whereas control group were nebulized with normal saline. All neonates were accessed for serial respiratory distress score (Downe's score), requirement of oxygen (in days), duration of neonatal intensive care unit stay. Budesonide nebulization in meconium aspiration results in significant early improvement in general condition (early improvement in respiratory distress and early normalization of Downe's score) of the newborn with lesser oxygen requirement, thus early discharge from NICU but has no impact on final outcome[7]

In a study by Suresh R et al, effect of nebulized budesonide in improving the clinical outcome of neonates with meconium aspiration syndrome done in Mysore Medical College and Research Institute, Department of Pediatrics, Mysore; involving a total of 60 patients with diagnosis of MAS were admitted to the NICU from August to October 2013. They found that the baseline clinical profile of both the groups were similar. Duration of respiratory distress in days (2.63 vs 5.24 p=0.0493), duration of oxygen dependency (2.37 vs 4.94 p=0.0406), duration of hospital stay (7.58 vs 10.47 p=0.0430), time taken for

achievement of full feeds (3.79 vs 8.76 p-0.0002) and the need for mechanical ventilation (0 vs 0.2 p=0.0356) were statistically less in budesonide treated group as compared to the controls. Incidence of sepsis is similar in both the groups. Complications were similar in both the groups and no specific adverse effects were noted in the steroid treated group[71]. In a study by Daniela Mokra et al in the year 2011 in a review article concluded that glucocorticoid may be beneficial particularly in severe form of MAS with apparent lung edema, pulmonary vasoconstriction and inflammation[4].

Ward MC et al in the year 2009 in a review article in the Cochrane collaboration concluded that the small number and sample sizes of randomized control trials undertaken to date, and the mortality and morbidity associated with MAS itself, the limited information available to date suggest early parenteral dexamethasone would be an appropriate intervention for further study[5].

In a study by Sriparna Basu et al, role of steroids on the clinical course and outcome of meconium aspiration syndrome a randomized controlled trial conducted in three groups over a period of 1 year i.e., 2007, at department of Pediatrics at Banaras Hindu University, Varanasi. Group A (control, n =33), group B (n = 34) received i.v methylprednisolone of 0.5mg/kg/day in two divided doses and group C (n=32) received nebulized budesonide in a dose of 50µg in 2.5 ml of normal saline. This was given for a period of 7 days starting after 24hrs and found that period of oxygen dependency and duration of hospital stay was significantly less in the steroid treated groups. Also enteral feeding and radiological clearance of chest was achieved earlier in steroid treated groups[2].

In a study by Tripathi S et al, effect of steroids on the clinical course and outcome of neonates with meconium aspiration syndrome, a double blinded randomized controlled trial conducted over a period of one year in 2007, in the neonatal unit of the Lady Hardinge Medical College and associated Kalawati Saran Children's hospital. 51 babies of MAS which were randomly distributed into three groups; control, systemic and nebulized steroids. Methyl prednisolone was given i.v. in dose of 0.5 mg/kg/day in two divided doses. Budecort was given by nebulization in dose of 50 microgram 12 hourly. Infants were assessed in terms of duration of stay, oxygen dependence, X-ray clearances and also assessed for short term adverse effects. There was statistically significant difference in the duration of stay, duration of oxygen dependence and radiological clearance. The use of steroids was not associated with an increased incidence of sepsis[64].

In a study by Yeh TF et al, hydrocortisone therapy in meconium aspiration syndrome: a double blinded controlled study, to evaluate the efficacy of glucocorticoids in the treatment of infants with meconium aspiration syndrome in 1977. Thirty-five infants were included in the study. No significant difference in requirement for assisted ventilation or in survival were domonstrated between the groups. In control group, a significant decrease (p less than 0.01) in respiratory distress score was found at 48 to 72 hours of age; in hydrocortisone

group, it was seen only after 72 hours. The infants in the hydrocortisone group took a significantly longer (p less than 0.01) period of time to wean to room air than those in the control group (68.9 ± 9.6 hours vs 36.6 ± 6.9 hours). On the basis of these observations, hydrocortisone is not recommended for treatment of MAS[63].

To conclude, steroids doesn't alter the outcome of meconium aspiration syndrome (MAS) in terms of oxygen dependency, duration of hospital stay, morbidity and mortality.

3

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