

## **Intralipid treatment for newborns with meconium stained amniotic fluid (MSAF)**

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### **Abstract**

One in every seven pregnancies ends with meconium-stained amniotic fluid (MSAF). MSAF can be harmful to the newborn with short and long-term sequelae.

A new treatment of Intravenous Intralipid is first suggested for MSAF.

**Key words : meconium stained amniotic fluid (MSAF) , Intralipid**

### **MAS and MSAF**

One in every seven pregnancies ends with meconium-stained amniotic fluid (MSAF). MSAF can be harmful to the newborn with short and long-term sequelae. This study (1) was aimed to find out the incidence, predictors, onset and severity of respiratory distress among vigorous babies born through meconium stained amniotic fluid which may or may not be evident at birth.

This study (1) included one hundred and forty-one vigorous babies born through meconium stained amniotic fluid, of which 36.9% (52) babies developed respiratory distress. Of the 52 babies who developed respiratory distress 19.23%(10 babies) developed meconium aspiration syndrome (MAS). In this study, it was observed factors like caesarean section and thick meconium increased risk of respiratory distress in the neonates born through meconium stained amniotic fluid who were vigorous.

98.07% (51 babies) developed respiratory distress at birth or within one hour of life. All the babies who developed MAS had mild or moderate form of MAS. None of the babies required assisted ventilation. Risk factors like thick meconium, caesarean section showed significant increase in the incidence of

respiratory distress. Therefore intrapartum monitoring and timely intervention can prevent the complications of MAS (1).

In developing countries, meconium aspiration syndrome (MAS) is an important cause of morbidity and mortality among neonates. The concepts of pathophysiology and management of meconium stained amniotic fluid (MSAF) and meconium aspiration syndrome have undergone tremendous change in recent years. Routine intranatal and postnatal endotracheal suctioning of meconium in vigorous infants is no longer recommended. Recent studies have challenged its role even in non-vigorous infants. Supportive therapy like oxygen supplementation, mechanical ventilation and intravenous fluids are the cornerstone in the management of meconium aspiration syndrome. Availability of surfactant, inhaled nitric oxide, high frequency ventilators and extracorporeal membrane oxygenation has made it possible to salvage more infants with meconium aspiration syndrome (2).

### **Endotracheal suction**

To evaluate the effect of 'No endotracheal suction' on occurrence of meconium aspiration syndrome (MAS) and/or all-cause mortality in non-vigorous neonates born through meconium stained amniotic fluid (MSAF).

This pilot (3) randomized controlled trial enrolled term non-vigorous neonates ( $\geq 37$  weeks) born through MSAF. Neonates randomized to 'No Endotracheal suction group' ('No ET' Group; n=88) did not undergo endotracheal suction before the definitive steps of resuscitation. Neonates randomized to 'Endotracheal suction group' ('ET' Group; n=87) underwent tracheal suction as part of the initial steps as per the current NRP recommendations. The primary outcome was occurrence of MAS and/or death. Secondary outcome variables were duration and severity of respiratory distress, need for respiratory support, development of hypoxic ischemic encephalopathy (HIE) and duration of oxygen therapy and hospitalization.

Baseline characters including birth weight and gestational age were similar between the two groups. MAS was present in 23 (26.1%) vs. 28 (32.2%) neonates in 'No ET' and 'ET' groups respectively (OR 0.4 (0.12-1.4); p=0.14) with 4 (4.6%) and 9 (10.34%) deaths amongst these neonates with MAS in respective groups (OR 0.75 (0.62-1.2); p=0.38). Other parameters like

severity and duration of respiratory distress, need for respiratory support, incidence of HIE, duration of oxygen therapy and duration of hospitalization were comparable.

This study demonstrates that it is feasible to randomize non-vigorous infants born through meconium stained liquor to receive or not receive endotracheal suction (3).

### **Antibiotics**

To identify and assess the characteristics, risk and outcome of neonates treated with empiric antibiotics for suspected early onset sepsis (EOS).

This is a retrospective study (4) conducted at a Malaysian government hospital. Records of neonatal patients admitted within 72 h of life and prescribed with empirical antibiotic therapy for suspected EOS were reviewed.

Three hundred and twenty-three cases met the inclusion criteria and were divided into gestational age (premature < 36 weeks; term  $\geq$  37 weeks) and birth weight (low birth weight (LBW) < 2.5 kg; normal body weight (NBW)  $\geq$  2.5 kg) groups. Premature (n = 197) and LBW (n = 194) neonates required significantly longer hospital stay, a higher degree of ventilator support and more surfactant ( $p = 0.001$ ). More than 90.0% of premature and LBW neonates were diagnosed with respiratory distress syndrome, congenital pneumonia and presumed sepsis. Term (n = 123) and NBW (n = 129) neonates had greater maternal risk factors, especially meconium-stained amniotic fluid (MSAF) and perinatal asphyxia. The incidence of demonstrated EOS was 3.1%. Crystalline penicillin plus gentamicin was the standard therapy for all groups and was started within 24 h of life, with a mean treatment duration of ~4 days. The treatment success rate was 89.0%, and only LBW neonates showed a higher risk of overall treatment failure (OR = 3.75; 95% CI: 1.22-11.53). Seventy-four percent of term and NBW neonates discharged well, while 42.0% of premature and LBW neonates required referral.

Crystalline penicillin plus gentamicin prescribed within 24 h of life is effective in the prevention of EOS. However, low birth weight neonates have a higher risk of treatment failure (4).

## **Oronasopharyngeal suction**

Oronasopharyngeal suction (ONPS) is regularly performed in neonates at delivery in many hospitals across the country today (5). Although ONPS is a technique that has essentially become habitual for most obstetricians, its theorized usefulness to help promote expeditious lung aeration after delivery by removal of amniotic fluid, meconium, mucus and blood that may otherwise be aspirated by the newborn, is currently not recommended. ONPS can cause vagal stimulation-induced bradycardia and thus hypercapnea, iatrogenic infection due to mucous membrane injury, and development of subsequent neonatal brain injury due to changes in cerebral blood flow regulation, particularly in premature infants. Multiple studies that have been performed comparing routine use of ONPS to no intervention controls indicate that newborns receiving ONPS took a longer time to achieve normal oxygen saturations, caused apneic episodes, and caused disturbances in heart rate (mainly bradycardia) compared to the control groups. Although the ONPS groups revealed no significantly different APGAR scores at 1 and 5 minutes, the ONPS groups took longer than the control group to reach an arterial oxygen saturation greater than or equal to 92% in the first minutes of life. Currently, Neonatal Resuscitation Program guidelines discourage the use of or meconium-stained amniotic fluid and in the absence of obvious obstruction. Furthermore, this manuscript highlights various literature sources revealing that the routine use of ONPS at the time of delivery can cause more harm than good, if any good at all (5).

Evidence about IP-OP suction and selective tracheal intubation in meconium stained neonates is from developed countries. Little information is available about their role in developing countries with high incidence of meconium staining and MAS. This randomized trial (6) was planned to evaluate the effectiveness of IP-OP suction in meconium stained term neonates on prevention of MAS and reduction of its severity.

Out of 540 meconium stained full term, cephalic presentation, singleton neonates without major congenital malformations born from June'08 to January'09, 31 were excluded and 509 randomized. In the intervention group IP-OP suction was done at the time of delivery of head using a 10 Fr suction catheter with a negative pressure of 100 mmHg. No IP-OP suction was performed in control group. All neonates with MSAF were assessed as

vigorous or non-vigorous after birth and provided care as per NRP guidelines 2005.

Two hundred and fifty three neonates were randomized to IP-OP suction and 256 to no IP-OP suction. Eighty-two neonates (16%) developed MAS, the primary outcome parameter, with 40 infants in the intervention group (15.8%) and 42 (16.4%) in the non-intervention group (RR 0.86, 95% CI 0.60-1.54). Incidence of severe MAS was comparable (3.55% vs. 2.34%) (P value=0.40). Other variables like requirement of oxygen >48 h (9.8% vs. 10.5%) and mortality (2.7% vs. 1.7%) were also comparable.

IP-OP suctioning did not reduce the incidence or severity of MAS even in a setting of high incidence of MAS in a developing country. The mortality in two groups was comparable (6).

### **Gastric lavage**

Neonates born with meconium stained amniotic fluid (MSAF) can develop feed intolerance during first few days of post -natal period. A randomized controlled trial was conducted with the objectives of to find out the incidence of feed intolerance in vigorous neonates with MSAF who received gastric lavage (GL) as compared to those in whom it was not performed.

This was a randomized controlled trial on 500 neonates satisfying the inclusion criteria, 230 were allocated to GL and 270 to no lavage group through computer generated random numbers.

No significant difference in the incidence of vomiting was found between GL and no lavage group (8.7 % vs 11.5 %, p = 0.305). Feed intolerance had no relationship with gestational age, gender, birth weight and mode of delivery. No neonates of GL group developed any complications related to the procedure.

Thus, it may be concluded that gastric lavage is not required in neonates born with MSAF (7).

### **Endotracheal suctioning**

To assess whether endotracheal suctioning of nonvigorous infants born through meconium stained amniotic fluid (MSAF) reduces the risk and complications of meconium aspiration syndrome (MAS).

Term, nonvigorous babies born through MSAF were randomized to endotracheal suction and no-suction groups (n=61 in each). Risk of MAS, complications of MAS and endotracheal suction, mortality, duration of neonatal intensive care unit stay, and neurodevelopmental outcome at 9 months were assessed.

Maternal age, consistency of meconium, mode of delivery, birth weight, sex, and Apgar scores were similar in the groups. In total, 39 (32%) neonates developed MAS and 18 (14.8%) of them died. There were no significant differences in MAS, its severity and complications, mortality, and neurodevelopmental outcome for the 2 groups. One infant had a complication of endotracheal suctioning, which was mild and transient.

The current practice of routine endotracheal suctioning for nonvigorous neonates born through MSAF should be further evaluated (8).

### **Prophylactic antibiotics**

The objective of the study (9) was to evaluate the effect of administering prophylactic antibiotics on the development of neonatal sepsis in term neonates born through meconium-stained amniotic fluid (MSAF). Two hundred and fifty eligible neonates were randomized to study group (Antibiotic group-receiving first-line antibiotics for 3 days) and control group (No Antibiotic group). Both groups were evaluated clinically and by laboratory parameters (sepsis screen and blood cultures) for development of sepsis. All neonates were monitored for respiratory, neurological, and other systemic complications and received supportive treatment according to standard management protocol of the unit. One hundred and twenty one neonates were randomized to 'Antibiotic' group and 129 to 'No Antibiotic' group. The overall incidence of suspect sepsis was 9.6 % in the study population with no significant difference between 'No Antibiotic' and 'Antibiotic' groups (10.8 vs. 8.2 %,  $p = 0.48$ , odds ratio (OR) 0.74, 95 % confidence interval (CI) 0.32-1.73). Incidence of culture-proven sepsis was also not significantly different between the two groups (5.42 vs. 4.13 %,  $p = 0.63$ , OR 0.75, 95 % CI 0.23-2.43). The incidence of mortality, meconium aspiration syndrome, and other complications was comparable amongst the two groups.

Routine antibiotic prophylaxis in neonates born through MSAF did not reduce the incidence of sepsis in this study population (9).

## **Chorioamnionitis**

Chorioamnionitis is more likely to occur when meconium-stained amniotic fluid (MSAF) is present. Meconium may enhance the growth of bacteria in amniotic fluid by serving as a growth factor, inhibiting bacteriostatic properties of amniotic fluid. Many adverse neonatal outcomes related to MSAF result from meconium aspiration syndrome (MAS). MSAF is associated with both maternal and newborn infections. Antibiotics may be an effective option to reduce such morbidity.

The objective of this review (10) is to assess the efficacy and side effects of prophylactic antibiotics for MSAF during labour in preventing maternal and neonatal infections.

We (10) searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2014).

Randomised controlled trials (RCTs) comparing prophylactic antibiotics with placebo or no treatment during labour for women with MSAF.

Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy.

We (10) included two studies with 362 pregnant women. Both studies compared ampicillin-sulbactam (N = 183) versus normal saline (N = 179) in pregnant women with MSAF. Prophylactic antibiotics appeared to have no statistically significant reduction in the incidence of neonatal sepsis (risk ratio (RR) 1.00, 95% CI 0.21 to 4.76), neonatal intensive care unit (NICU) admission (RR 0.83, 95% CI 0.39 to 1.78) and postpartum endometritis (RR 0.50, 95% CI 0.18 to 1.38). However, there was a significant decrease in the risk of chorioamnionitis (RR 0.36, 95% CI 0.21 to 0.62). No serious adverse effects were reported. Drug resistance, duration of mechanical ventilation and duration of admission to NICU/hospital were not reported. Most of the domains for risk of bias were at low risk of bias for one study and at unclear risk of bias for the other study. The quality of the evidence using GRADE was low for neonatal sepsis, postpartum endometritis, and neonatal mortality and morbidity prior to discharge (Neonatal intensive care admissions) and of moderate quality for chorioamnionitis.

Current evidence indicates that compared to placebo, antibiotics for MSAF in labour may reduce chorioamnionitis. There was no evidence that antibiotics could reduce postpartum endometritis, neonatal sepsis and NICU admission.

This systematic review identifies the need for more well-designed, adequately powered RCTs to assess the effect of prophylactic antibiotics in the incidence of maternal and neonatal complications (10).

The role of gastric lavage in preventing retching, vomiting and secondary meconium aspiration syndrome in neonates with meconium-stained amniotic fluid is uncertain, and no there are no definitive guidelines.

To evaluate the effect of gastric lavage in preventing retching, vomiting and secondary meconium aspiration syndrome in neonates with meconium-stained amniotic fluid.

This was an open-label, parallel, randomized controlled trial conducted in the labour room, postnatal and neonatal wards of a tertiary-care teaching hospital. Vigorous neonates of  $\geq 34$  weeks gestation with meconium-stained amniotic fluid were randomised into two groups using block randomisation. Infants requiring oxygen, in respiratory distress or with major congenital malformations were excluded. Infants in the study group received elective gastric lavage in the labour room after initial stabilisation. No gastric lavage was done in the control group. The newborns were assessed for retching, vomiting and secondary meconium aspiration syndrome in the first 48 hrs of life or until discharge from the hospital, whichever was later.

A total of 267 newborns were randomly assigned to the gastric lavage group and 269 to the no gastric lavage group. There were no statistical differences in overall feeding between the two groups (6.74% vs 10.78%). Feeding of two newborns in the no-lavage group had to be omitted for the initial few hours because of vomiting; this did not happen in any newborn in the lavage group. No newborn in either group developed secondary meconium aspiration syndrome.

Gastric lavage in newborns with meconium-stained amniotic fluid does not prevent or reduce the occurrence of feeding problems or secondary meconium aspiration syndrome (11).

### **Amnioinfusion**

Amnioinfusion is thought to dilute meconium present in the amniotic fluid and so reduce the risk of meconium aspiration.



To assess the effects of amnioinfusion for meconium-stained liquor on perinatal outcome.

We (12) searched the Cochrane Pregnancy and Childbirth Group's Trials Register (1 December 2013).

Randomised trials comparing amnioinfusion with no amnioinfusion for women in labour with moderate or thick meconium staining of the amniotic fluid.

Three review authors independently assessed eligibility and trial quality, and extracted data.

Fourteen studies of variable quality (4435 women) are included. Subgroup analysis was performed for studies from settings with limited facilities to monitor the baby's condition during labour and intervene effectively, and settings with standard peripartum surveillance. Settings with standard peripartum surveillance: there was considerable heterogeneity for several outcomes. There was no significant reduction in the primary outcomes meconium aspiration syndrome, perinatal death or severe morbidity, and maternal death or severe morbidity. There was a reduction in caesarean sections (CSs) for fetal distress but not overall. Meconium below the vocal cords diagnosed by laryngoscopy was reduced, as was neonatal ventilation or neonatal intensive care unit admission, but there was no significant reduction in perinatal deaths or other morbidity. Planned sensitivity analysis excluding trials with greater risk of bias resulted in an absence of benefits for any of the outcomes studied. Settings with limited peripartum surveillance: three studies were included. In the amnioinfusion group there was a reduction in CS for fetal distress and overall; meconium aspiration syndrome (three studies, 1144 women; risk ratio (RR) 0.17, 95% confidence interval (CI) 0.05 to 0.52); perinatal mortality (three studies, 1151 women; RR 0.24, 95% CI 0.11 to 0.53) and neonatal ventilation or neonatal intensive care unit admission. In one of the studies, meconium below the vocal cords was reduced and, in the other, neonatal encephalopathy was reduced.

Amnioinfusion is associated with substantive improvements in perinatal outcome only in settings where facilities for perinatal surveillance are limited. It is not clear whether the benefits are due to dilution of meconium or relief of oligohydramnios. In settings with standard peripartum surveillance, some non-substantive outcomes were improved in the initial analysis, but sensitivity analysis excluding trials with greater risk of bias eliminated these differences. Amnioinfusion is either ineffective in this setting, or its effects are masked by

other strategies to optimise neonatal outcome. The trials reviewed are too small to address the possibility of rare but serious maternal adverse effects of amnioinfusion (12).

### **Respiratory distress**

This study (13) aimed to find out incidence, predictors, onset and severity of respiratory distress including meconium aspiration syndrome (MAS) among vigorous neonates born through meconium stained amniotic fluid (MSAF), which may or may not be evident at birth.

Two hundred ninety vigorous neonates were studied. Data were collected on perinatal risk factors, clinical course and development of respiratory distress. Predictors of respiratory distress were identified by logistic regression and a score based on adjusted OR was assigned for each. Diagnostic performance of the score (0-24) was assessed on another 247 vigorous neonates using receiver operator characteristic analysis (ROC).

Respiratory distress developed in 97(33.4 %) infants, MAS in 75(25.9 %). The distress appeared within 12 h in 97.9 %, was severe in only 21.7 %. Of 10 risk factors significantly associated with respiratory distress, seven entered in regression analysis. Fetal distress(adj OR = 11.8; 95%CI = 6.2-22.5), prolonged labor(adj OR = 5.2; 95%CI = 2.5-10.7), and absent/poor cry(adj OR = 5.6; 95%CI = 2.4-13.3) were identified as independent predictors; each assigned a score of 12, 6 and 6, respectively. To predict respiratory distress, a cut-off score of 9 points had sensitivity-74.1 % (95%CI = 63.3 %-82.7 %), specificity-84.6 % (95 % CI = 77.9 %-89.6 %), positive predictive value- 71.6 % (95%CI = 60.8 %-80.4 %), negative predictive value- 86.2 % (95 % CI = 79.6 %-90.9 %), likelihood ratio (LR) + ve 4.8(95%CI = 3.3-7.0) and LR-ve 0.3(95%CI = 0.2-0.4).

Respiratory distress occurred in one third neonates, mostly had onset within 12 h of birth, and it was mild to moderate in majority. Fetal distress, prolonged labor, and absent/poor cry predicted respiratory distress and were validated. However, larger studies in different settings are required to confirm its utility (13).

## **Feed intolerance**

To compare reduction in incidence of feed intolerance in neonates born with meconiumstained amniotic fluid (MSAF) by use of gastric lavage to those who did not receive lavage.

This Randomized controlled trial was conducted in all vigorous newborns delivered through MSAF, with birth weight  $\geq 1800$  g and gestation  $\geq 34$  wk. In the lavage group, gastric lavage with 10 ml/kg of normal saline was done.

Twelve neonates in the lavage group (n = 124) developed feed intolerance compared to 16 neonates in control group (n = 120), (p = .309; OR 0.69; 95%CI 0.27-1.58). No difference in any other morbidity was noted.

Gastric lavage in neonates with MSAF does not reduce feed intolerance, irrespective of thickness of MSAF and it confers no advantages (14).

## **Intralipid**

The optimal dosing regimens of lipid emulsion, epinephrine, or both are not yet determined in neonates in cases of local anaesthetic systemic toxicity (LAST).

Newborn piglets received levobupivacaine until cardiovascular collapse occurred. Standard cardiopulmonary resuscitation was started and electrocardiogram (ECG) was monitored for ventricular tachycardia, fibrillation, or QRS prolongation. Piglets were then randomly allocated to four groups: control (saline), Intralipid(®) alone, epinephrine alone, or a combination of Intralipid plus epinephrine. Resuscitation continued for 30 min or until there was a return of spontaneous circulation (ROSC) accompanied by a mean arterial pressure at or superior to the baseline pressure and normal sinus rhythm for a period of 30 min.

ROSC was achieved in only one of the control piglets compared with most of the treated piglets. Mortality was not significantly different between the three treatment groups, but was significantly lower in all the treatment groups compared with control. The number of ECG abnormalities was zero in the Intralipid only group, but 14 and 17, respectively, in the epinephrine and epinephrine plus lipid groups ( $P < 0.05$ ).

Lipid emulsion with or without epinephrine, or epinephrine alone were equally effective in achieving a return to spontaneous circulation in this model of

LAST. Epinephrine alone or in combination with lipid was associated with an increased number of ECG abnormalities compared with lipid emulsion alone (15).

This study (16) aimed to compare the effect of 2 lipid emulsions (LEs), a medium-chain triglyceride (MCT)/ $\omega$ -3-polyunsaturated fatty acid (PUFA)-containing LE and a soybean-based LE, on the incidence of neonatal cholestasis, bronchopulmonary dysplasia (BPD), and lipid profile of preterm infants. Patients and

In this prospective, observational study, 2 groups of preterm neonates, the very low birth weight (VLBW) (n = 129) and the low birth weight (LBW) groups (n = 153), which received parenteral LEs for at least 7 days, were included. Infants received either MCT/ $\omega$ -3-PUFA-containing LE (SMOFlipid, subgroup I) or soybean-based LE (Intralipid, subgroup II) according to the attending neonatologist's preference and availability. Full biochemical assessment was performed on days of life 15, 30, and 45 and on discharge.

Of the VLBW infants, 7.4% and 13.3% of infants in subgroups I and II, respectively, developed cholestasis (P = .39; odds ratio [OR], 0.52; 95% confidence interval [CI], 0.15-1.76). The duration of LE administration was independently associated with cholestasis (P < .001; OR, 0.925; 95% CI, 0.888-0.963). The maximum amounts of lipids administered ranged between 1.6 and 3.6 g/kg/d in both VLBW subgroups. The VLBW subgroup I had lower incidence of BPD, lower alkaline phosphatase and phosphate, higher high-density lipoprotein (HDL), and lower cholesterol-to-HDL ratio on discharge than the VLBW subgroup II. The type of LE was independently associated with BPD and alkaline phosphatase. In the LBW group, the type of LE was not associated with clinical and biochemical parameters.

In VLBW infants, the MCT/ $\omega$ -3-PUFA-containing LE administration is associated with decreased BPD and more favorable lipoprotein profile. Although a trend toward a lower incidence of cholestasis was observed, a preventive effect of MCT/ $\omega$ -3-PUFA-containing LE on parenteral nutrition-associated cholestasis is not supported (16).

We (17) report a case of bupivacaine-induced cardiotoxicity in a neonate following caudal epidural block under general anesthesia for urologic surgery. Prompt recognition of the complication allowed early intervention with both standard resuscitative measures and administration of 20% Intralipid(®) , resulting in a good outcome (17).

To review the current state of the science regarding intravenous fat emulsions (IVFEs), with an emphasis on their safety profile.

Articles were identified via a search of the MEDLINE database, including publications from 1979 to December 2009, using a search string that included the terms parenteral nutrition, lipid emulsion, fat emulsion, IVFE, safety, adverse effect, neonate intralipid, and terms describing a range of specific adverse events (AEs) such as pancreatitis.

We (18) selected articles that allowed us to compare the results of clinical trials involving delivery of medications via IVFEs with the historical use and effects of IVFEs in parenteral nutrition, with an emphasis on AEs. We (18) focused on 2 drugs in current use that are administered intravenously in lipid emulsions: propofol and clevidipine.

Clearance of the fat particles in IVFEs is mediated by the enzyme lipoprotein lipase. AEs are more likely if the rate or duration of IVFE administration exceeds the enzyme's clearance capacity. AEs are also more likely after administration of a 10% IVFE formulation than a 20% formulation, because the higher concentration of free phospholipid in the 10% formulation interferes with lipoprotein lipase activity. AEs can be reduced by administering IVFEs at a dosage  $\leq 2.5$  g/kg/day and at a rate  $\leq 0.11$  g/kg/h. The anesthetic agent propofol, which is formulated in a 10% IVFE, has been used clinically for 25 years. Typical AEs associated with propofol use include infection, high plasma triglyceride concentrations, and pancreatitis. Recent clinical trials involving clevidipine, which is formulated in a 20% IVFE, have demonstrated a low rate of lipid-related AEs.

The results of this review demonstrate that IVFEs are well tolerated when administered in accordance with guideline recommendations (18).

These findings suggest that most intralipid errors occur during the administration phase. This complex process can generate high opportunities for error directly related to the use of IV pumps. Nursing staff members are prone to making dosing errors while accurately programming the infusion devices, especially during times of high workload. The evening hours around shift change appeared most vulnerable to such errors occurring. A further analysis to include error rates as a function of error opportunities is critical. The tracking and tallying of such opportunity for error can be accomplished using smart pump technology. A detailed analysis of the existing intralipid administration workflow process will guide the overall

strategy of an error prevention plan. Understanding the nursing workload as a function of time of day and census is essential. These mission-critical tasks often require the hard work of a dedicated task force, the commitment of the hospital leadership, and cooperation from the health care providers (19).

In 1998 (20) it was first showed that intravenous Intralipid could prevent or improve resuscitation from cardiovascular collapse by severe bupivacaine overdose in rats. Since then published examples now include toxicities related to verapamil, diltiazem, amlodipine, quetiapine and sertraline, haldoperidol, lamotrigine, olanzapine, propranolol, atenolol, nevigolol, doxepin, dosulepin, imipramine, amitriptyline, glyosphate herbicide, flecainide, venlafaxine, moxidectin, and others. Amniotic fluid embolism (AFE) is a rare but potentially catastrophic obstetric emergency. Despite earlier recognition and aggressive treatment, morbidity and mortality rates remain high. An estimated 5% - 15% of all maternal deaths in Western countries are due to AFE. The pathophysiology of AFE is not completely understood. AFE most commonly occurs during labor, delivery, or the immediate postpartum period.

However, it has been reported to occur up to 48 h postpartum. Pulmonary hypertension and right heart strain/failure may be the result of physical amniotic fluid debris in the pulmonary vasculature or, perhaps more likely, result from circulating pulmonary vasoconstrictive mediators. Therapy with Intralipid in male rats resulted in 100% survival and prevented Pulmonary arterial hypertension-induced right ventricular failure by preserving right ventricular pressure and right ventricular ejection fraction and preventing right ventricular hypertrophy and lung remodeling. In preexisting severe Pulmonary arterial hypertension, Intralipid attenuated most lung and right ventricular abnormalities.

The beneficial effects of Intralipid in Pulmonary arterial hypertension seem to result from the interplay of various factors, among which preservation and/or stimulation of angiogenesis, suppression and/or reversal of inflammation, fibrosis and hypertrophy, in both lung and right ventricular, appear to be major contributors. In conclusion, Intralipid not only prevents the development of Pulmonary arterial hypertension and right ventricular failure but also rescues preexisting severe Pulmonary arterial hypertension. Intralipid treatment is a new treatment for AFE (amniotic fluid embolism) which was never suggested before (20).

Amniotic fluid embolism (AFE) is a rare and often fatal complication that occurs in the peripartum period. We (21) present a patient with an AFE who developed disseminated intravascular coagulation and cardiovascular collapse who may have benefitted from intravascular lipid emulsion rescue.

This is the first published case in which lipid emulsion was a part of the successful treatment of AFE (21).

### **Conclusion**

A new treatment of Intravenous Intralipid is first suggested for MSAF.

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