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INTRALIPID Rescue of Amniotic Fluid Embolism: from Theory to Existence

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Abstract

A 33-year-old women, gravida 7, para 4, status post 4 classical cesarean sections. She was admitted to elective cesarean section and bilateral tubal ligation at 36 week's gestation. General anesthesia was chosen by the patient. The time from anesthesia induction to fetal delivery was 8 minutes. Newborn was Apgar score 8/9, weight 2570, pH-7.26. Anesthesia stuff reported suddenly desaturation till 76%, blood pressure decreased till 45/20, increased pulse 135 per minutes and difficulty in ventilation immediately after fetal delivery. Solution Intralipid 20%, 1.5 mL per kg (100 mL), starting with a bolus, and 2 unit transfusions of Packed Red Blood Cells (PRBCs) were started. ECMO team and TEE stuff were called.

After a loading dose of 100 ml during 30 minutes of Intralipid Solution, a maintenance of 0.5 mL per kg would be extended. The condition of the patient continued to be difficult with a substantial improvement of Blood Pressure 80/40, but pulse 138 per minutes, ABG-pH 7.26, pO_2-75, pCO_2-30, Lactate 5.6, HCO_3-12, BE-(-12). Coagulation products like 5 units of Cryoprecipitate, 5 units of Platelets, 3 units of FFP and Calcium Gluconate 1gm were started due to some vaginal bleeding. Cardiovascular and Oxygenation parameters began to improve suddenly after 40 minutes from the beginning of the event, BP 105/55, Sao_2-100%, ABG- pO_2 519, and because of that the ECMO team was canceled and the patient was discharged home after 3 days in good health condition.

This is the second case report article publication of Intralipid rescue of a parturient suffering from Amniotic Fluid Embolism. Unlike the Baylor Scott and White Health, Temple, Texas case in which Intralipid was given as a LAST RESORT the Soroka, Beer Sheva case was given IMMEDIATELY according to the Eldor- Kotlovker theory. Based on these 2 breakthrough cases regarding the INTRALIPID TREATMENT FOR AFE it is firmly suggested to make it the gold standard of the AFE treatment WORLDWIDE.

Keywords: Amniotic Fluid Embolism, Intralipid, Lipid Emulsion.

Case Report

A 33-year-old women, gravida 7, para 4, status post 4 classical cesarean sections. The first cesarean section was done due to fetal macrosomia. The second C/S due to patient request. The third C/S was complicated of uterine rupture in area of uterine scar. The four C/S was reported severe abdominal adhesions. This pregnancy was placenta Previa with no bleeding. She was admitted to elective cesarean section

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and bilateral tubal ligation at 36 week's gestation. Celestone chrono dose was given 12 mg IM twice every 24 hours. Option of hysterectomy was discussed with the patient in the preoperative clinic. She was taken to operating room due to early labor contractions.

General anesthesia was chosen by the patient. Roles of rapid sequence induction were followed. The time from anesthesia induction to fetal delivery was 8 minutes. Newborn was Apgar score 8/9, weight 2570, pH -7.26. Anesthesia stuff reported suddenly desaturation till 76%, blood pressure decreased till 45/20, increased pulse 135 per minutes and difficulty in ventilation immediately after fetal delivery. CPR management was started including PCV, FiO_2-100%, fluid resuscitations, norepinephrine drip, CVP and AL insertion. The first ABG presented pH-7.19, pO_2-45, pCO_2-31, Lactate 4.5, HCO_3 14, B.E-(-12), Hct-18 Solution Intralipid 20%, 1.5 mL per kg (100 mL), starting with a bolus, and 2 unit transfusions of Packed Red Blood Cells (PRBCs) were started. ECMO team and TEE staff were called. The Cesarean Section procedure was completed. The surgery crew reported a well collapse of the uterus and bleeding 700 mL. After a loading dose of 100 mL during 30 minutes of Intralipid Solution, a maintenance of 0.5 mL per kg would be extended. The condition of the patient continued to be difficult with a substantial improvement of Blood Pressure 80/40, but pulse 138 per minutes, ABG-pH 7.26, pO_2-75, pCO_2-30, Lactate 5.6, HCO_3-12, BE-(-12). Coagulation products like 5 units of Cryoprecipitate, 5 units of Platelets, 3 units of FFP and Calcium Gluconate 1gm were started due to some vaginal bleeding. Cardiovascular and Oxygenation parameters began to improve suddenly after 40 minutes from the beginning of the event, BP 105/55, Sao_2-100%, ABG- pO_2 519, and because of that the ECMO team was cancelled. Preparations for transfer to Intensive Care Unit began but Gynecologic crew reported of massive vaginal bleeding with no clots along hemodynamic instability despite treatment and was decided to proceed with hysterectomy like the main source of bleeding. Massive blood transfusion includes 4 units of PRBCs, 6 units of FFP, 10 units of Cryoprecipitate and Platelets continued. Solution Intralipid 20% was discontinued after receiving 150 mL total. The hemodynamic condition of patient stabilized after hysterectomy and hemostasis and she was transferred to the Intensive Care Unit. The patient was discharged home after 3 days in good health condition.

Discussion

Agustin Conde-Agudelo and Roberto Romero conducted on 2009 an evidence-based review of information about amniotic fluid embolism (AFE). The estimated incidence of AFE is 1:15, 200 and 1:53, 800 deliveries in North America and Europe, respectively. The case fatality rate and perinatal mortality associated with AFE are 13-30% and 9-44%, respectively. Risk factors associated with an increased risk of AFE include advanced maternal age, placental abnormalities, operative deliveries, eclampsia, polyhydramnios, cervical lacerations, and uterine rupture. The hemodynamic response in AFE is biphasic, with initial pulmonary hypertension and right ventricular failure, followed by left ventricular failure. Promising therapies include selective pulmonary vasodilators and recombinant activated facto VIIa [1].

On 2012 Joseph Eldor and Vladimir Kotlovker first suggested the use of Intralipid in AFE: "In 1998 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, nevibolol, 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 hrs 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 vaso-constructive 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" [2].

On 2018 McBride [3] wrote that AFE "treatment is supportive": "Obstetric emergencies often require intensive care intervention. Amniotic fluid embolism is a rare, unpredictable, and often catastrophic complication of pregnancy that is suspected in a woman who experiences cardiac arrest after a cesarean section. The condition occurs in approximately 1 in 40,000 births and has an average case-fatality rate of 16%. This complication may result from activation of an inflammatory response to fetal tissue in the maternal circulation. Risk factors may include maternal age over 35 years and conditions in which fluid can exchange between the maternal and fetal circulations. The presentation is abrupt, with profound cardiovascular and respiratory compromise, encephalopathy, fetal distress, and

disseminated intravascular coagulopathy. Diagnosis is by exclusion and clinical presentation. Treatment is supportive, with a focus on reversal of hypoxia and hypotension, delivery of the fetus, and correction of coagulopathy. Staff debriefing and psychological support for the woman and family are vital."

On 2017 Lynch W, Mc Allister RK, Lay JF Jr and Culp WC Jr. published the first case report on Lipid Emulsion Rescue of Amniotic Fluid Embolism-Induced Cardiac Arrest. It was done on 2016 at the Department of Anesthesiology, Texas A&M University System Health Science Center College of Medicine, Baylor Scott & White Health, Temple, Texas.

"A 28-year-old otherwise healthy, nonsmoking, 76 kg primigravid woman presented at 41 weeks of gestation for vaginal misoprostol induction of labor. Initial examination and review of systems were unremarkable. After 6 hours, a labor epidural catheter was placed without complication, and a ropivacaine 0.2% epidural analgesic infusion was initiated at 10 mL/h. An oxytocin infusion was administered for labor augmentation, and an intrauterine pressure catheter was placed. Occasional fetal heart decelerations occurred soon afterward, and the oxytocin infusion was stopped with the resolution of decelerations. Bleeding was then noted from the epidural catheter site. The patient had no history of coagulopathy, and there was no bleeding from any other site. The epidural catheter site was inspected, and a pressure dressing was applied. An hour later, the slow hemorrhage from the epidural catheter site had continued and coagulation studies including prothrombin time (PT) with international normalized ratio (INR), fibrinogen, and d-dimer were performed. Late decelerations returned and vaginal examination showed complete dilation and complete effacement.

The neonate was then vaginally delivered with vacuum assistance resulting in a third-degree perineal laceration. The patient developed postpartum hemorrhage that did not improve despite oxytocin, misoprostol, carboprost, and methyl-ergonovine administration. The etiology of the hemorrhage was suspected to be coagulopathy. Coagulation studies showed an increased PT of 22.6 seconds and INR of 2.0 (normal range PT 11-14 seconds and INR 0.8-1.1). Disseminated intravascular coagulation was suspected. Additional IV catheters were placed, 2 units of cross matched red blood cells (RBCs) were ordered for transfusion, and intrauterine tamponade with a Bakri balloon was performed to attempt to slow the vaginal hemorrhage. A perineal laceration was repaired despite the fact that it was not considered to be the major source of hemorrhage. Forty-seven minutes after completion of transfusion of cross matched blood but before intensive care unit transfer, the patient suddenly reported dyspnea and angina and rapidly developed an altered mental status. The patient then became hypotensive and tachycardic. Tracheal intubation was performed emergently, facilitated by intravenous administration of 10 mg etomidate and 100 mg succinylcholine when maintaining cricoid pressure. The tracheal tube was placed easily with a grade I laryngoscopic view. Shortly thereafter, pulses were absent on femoral and carotid artery examination. The presumed diagnosis was AFE presenting with disseminated intravascular coagulation and cardiovascular collapse.

Advanced cardiac life support (ACLS) and cardiopulmonary resuscitation (CPR) were immediately initiated during which a femoral central venous catheter and radial arterial catheter were placed and 6 units of cross matched RBCs with 4 units of fresh frozen plasma were administered to treat ongoing vaginal hemorrhage. The arterial catheter waveform suggested adequate peripheral perfusion from chest compressions. Bedside rescue trans-esophageal echocardiography (TEE) revealed right heart strain with moderate tricuspid regurgitation, no obvious saddle embolus on mid esophageal short-axis view of the ascending aorta, and severely depressed left ventricular systolic function with adequate left ventricular end-diastolic volume as seen on the trans-gastric short-axis view of the left ventricle. A finding suspicious for a thrombus was seen in the inferior vena cava near the liver. This was a small, slightly echogenic irregularity within the inferior vena cava less than 1 cm in diameter. Despite several administrations of ACLS medications including vasopressin, sodium bicarbonate, calcium chloride, atropine, and a total of 6 mg epinephrine, the patient's heart rhythm fluctuated between profound bradycardia and asystole for a prolonged period of 40 minutes. Other diagnoses were considered such as local anesthetic systemic toxicity (LAST) despite the fact that her epidural analgesia infusion was well within the normal dosing range for ropivacaine and worked well providing effective analgesia throughout her labor.

An inspection of the infusion revealed the expected amount of ropivacaine left in the bottle and no evidence of pump malfunction. The patient received an initial 8 mL bolus of ropivacaine 0.2% totaling 16 mg followed by an infusion of 10 mL/h for 6 hours, totaling 120 mg over 6-hour period, well below the maximum recommended dose limit for ropivacaine (3 mg/kg). As a last resort, IV lipid 20% emulsion (1.5 mL/kg) was administered as a bolus. Within 30 to 90 seconds, the patient had return of spontaneous circulation, normal sinus rhythm, and dramatic improvement in left and right ventricular function, shown clearly by TEE. After several minutes, the patient's condition slowly deteriorated once again to asystole, at which time CPR was once again started and a second lipid emulsion bolus (1.5 mL/kg) was administered and followed with an infusion at 0.25 mL/kg/min. Within 30 to 60 seconds, the patient again had a return of spontaneous circulation with normal sinus rhythm. In addition, she also exhibited spontaneous movements of her extremities.

She was transferred to the intensive care unit where she regained consciousness and was able to follow commands. Lipid emulsion infusion was discontinued shortly after arrival. Initial coagulation studies revealed fibrinogen levels <60 mg/dL and d-dimer levels >20 μ g/mL (normal range fibrinogen 150-400 mg/mL and d-dimer <0.5 μ g/mL). Because of ongoing vaginal hemorrhage, she required an additional 6 units of RBCs, 5 units of fresh frozen plasma, 1 unit of platelets, and 2 units of cryoprecipitate. Initially,

she required vasopressor support with epinephrine and norepinephrine until hemostasis and hemodynamic stability were achieved later that evening. She was sedated and ventilated overnight and monitored closely. The patient developed profound reperfusion injuries in both hands with severe ischemic changes. In addition, she experienced acute renal failure that required 4 sessions of dialysis. The next day, sedation was discontinued, and the patient was extubated after meeting all extubation criteria.

The patient was fully oriented without any obvious neurologic sequelae. The epidural catheter had been left in place because of her coagulopathy but was removed on hospital day 3 after normalization of coagulation studies. Follow-up at 6 months revealed no neurologic sequelae other than modest sensory-related deficits in bilateral hands related to reperfusion tissue injury. After discharge, the patient was able to fully participate in her activities of daily living and care for her newborn. Further hematologic investigation revealed no evidence of any underlying coagulopathic or hyper-coagulopathic condition that may have provided alternative etiologies of the cardiovascular collapse" [4].

Unlike the Baylor Scott & White Health, Temple, Texas USA case in which the patient was under epidural anesthesia and received the Intralipid "as a last resort, IV lipid 20% emulsion (1.5 mL/kg) was administered as a bolus" the Soroka Medical Center, Beer Sheva, Israel case was under general anesthesia from the start of the Cesarean Section operation (no connection to epidural bupivacaine like in the Texas case) and received the Intralipid almost immediately.

The Soroka case was exactly done according to Eldor-Kotlovker theory of AFE treatment (from 2012). In conclusion, not as a "last resort" but as an "immediate" treatment in any case suspected for Amniotic Fluid Embolism.

Conclusion

This is the second case report article publication of Intralipid rescue of a parturient suffering from Amniotic Fluid Embolism. Unlike the Baylor Scott & White Health, Temple, Texas case in which Intralipid was given as a LAST RESORT the Soroka, Beer Sheva case was given IMMEDIATELY according to the Eldor- Kotlovker theory. Based on these 2 breakthrough cases regarding the INTRALIPID TREATMENT FOR AFE it is firmly suggested to make it the gold standard of the AFE treatment WORLDWIDE.

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