A Prospective Randomized Study On Maternal And Infant Outcomes Of Intrapartum Transcervical Amnioinfusion Versus Standard Obstetric Care For Parturients With Meconium Stained Amniotic Fluid: A Preliminary Report*

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ABSTRACT

Background: Amnioinfusion, or transcervical infusion of saline into the amniotic cavity, has been proposed as a method for reducing the risk of meconium aspiration syndrome.

Objective: This study aims to assess the effect of intrapartal amnioinfusion with meconium stained amniotic fluid on cesarean section rate, incidence of meconium aspiration syndrome, neonatal ICU admission, perinatal death and adverse maternal outcomes.

Methods: This study is a randomized controlled trial from June to September 2013, conducted in the service wards of a university hospital. The study population consists of parturients 19-45 years old with singleton term low-risk pregnancies, in cephalic presentation, with cervical dilatation at 2-6 cm, with ruptured membranes showing meconium stained amniotic fluid.

Results: Meconium aspiration syndrome occurred in one infant in the amnioinfusion group and in three infants in the control group (9% vs. 25%). There was a lower rate of neonatal pneumonia and neonatal sepsis in the treatment arm (0% vs. 8% and 9% vs. 17%, respectively). There were no perinatal deaths in both groups. Neonatal ICU admission was seen less in the treatment arm (9% vs. 25%) The cesarean section rate did not differ significantly in both groups (9% vs. 8%). Maternal morbidity was seen less in the treatment group. None of the patients in the amnioinfusion arm had fever while two patients in the control group had pyrexia (0% vs. 17%). Hospital stay was also shorter for patients in the treatment group with an average duration of 3 days, as opposed to 4 days in the control arm.

Conclusion: Amnioinfusion is a relatively simple technique of reducing perinatal and maternal morbidity in patients with meconium stained amniotic fluid. Although this study did not show any significant difference between the two groups, there is a trend towards better neonatal outcomes and decreased maternal morbidity with amnioinfusion.

Keywords: amnioinfusion, intraamnionic saline infusion, meconium, meconium aspiration syndrome

INTRODUCTION

Meconium is a viscous sticky dark green substance containing gastrointestinal secretions, bile, bile acids, mucus, pancreatic juice, blood, swallowed vernix caseosa, lanugo, and cellular debris. Meconium stained amniotic fluid during labor is increasingly encountered in clinical practice, seen in 7% to 22% of pregnancies.[1] Meconium aspiration syndrome (MAS) complicates 1.7% to 35.8% of these deliveries.[2,4,12] Meconium aspiration may occur before birth or during the birth process. MAS requiring intubation occurs at higher rates in pregnancies beyond 40 weeks. Thirty-four percent of all MAS cases born after 40 weeks required intubation compared to 16% prior to 40 weeks.[3] In our institution, meconium stained amniotic fluid has complicated 3.8% of the obstetric admissions in the past year. There were 41 cases of meconium aspiration syndrome in our institution in the past year. Twelve deaths among these 41 were recorded.

The mechanism of meconium passage in the term and post-term fetus has two prevailing theories: 1) normal maturation of the gastrointestinal tract results in meconium passage, and 2) acute hypoxic events would lead to parasympathetic stimulation of the fetal bowel, followed by premature, stress-related bowel movements into the amniotic fluid.[2]

The passage of meconium in utero is associated with a significant increase in perinatal morbidity and mortality. Of note is an increased incidence of meconium aspiration syndrome (MAS), a potentially fatal hypoxic condition due to mechanical obstruction of the bronchioles and chemical pneumonitis.[5] Furthermore, independent of the conditions that lead to meconium passage, presence of meconium may subsequently cause complications, such as meconium-associated vascular necrosis of umbilical and placental chorionic vessels, inhibition of neutrophil oxidative burst and phagocytosis facilitating growth of

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pathogens within the amniotic fluid and subsequent intrauterine infection, and vasoconstrictive activity on the placental vasculature.[18]

The diagnosis of meconium rests on visual observation of greenish fluid discoloration. There is no definitive test that confirms the clinical impression of meconium in amniotic fluid or on histopathological specimen (ie, immunohistochemistry). Attempts have been made to identify the material chemically by establishment of characteristic spectrophotometric absorbance peaks (which are typically in the 405–415 nm range). However, because of the variable composition of meconium and the similarity with other blood breakdown products, this technique is imperfect for evaluating amniotic fluid samples.[20]

Obstetricians are faced with dilemmas in meconium staining management especially in under-resourced settings such as ours, where facilities such as continuous cardiotocographic monitoring and fetal scalp blood pH measurements are not readily available.[4]

In the past 30 years, cesarean section rates have also continued to rise. The indications for performing this surgery have changed in recent years and continue to evolve in varying circumstances. Some common and important indications for cesarean sections include fetal distress, prolonged labor, malpresentation, multiple gestations, previous cesarean section and cesarean section upon request. Most of these are done to benefit the fetus, not the mother.[11]

In a developing country like ours with scarce resources, the morbidity and mortality associated with meconium staining is high. In our institution in the past year, the case fatality rate of babies with meconium aspiration syndrome is 29.27%. Because of such high morbidity and mortality rates, the obstetrician is prodded to subject the mother to cesarean section because of the relative lack of intrapartum monitoring facilities. This also increases maternal morbidity in terms of a longer hospital stay, delayed recovery and higher cost of treatment.

Routine prophylactic intrapartum oropharyngeal and nasopharyngeal suctioning have not been shown to reduce the risk of meconium aspiration syndrome.[4,6,7] Amnioinfusion, or transcervical infusion of saline into the amniotic cavity, has been proposed as a method for reducing the risk of MAS.[1,8]

Amnioinfusion was first described by Gabbe in 1976.[9] A chronic fetal rhesus monkey preparation was used in this investigation. Results showed that loss of amniotic fluid produced variable deceleration patterns while restoration of amniotic fluid volume eliminated such changes. However, it was only in 1983 when amnioinfusion was applied clinically. This was done by Miyazaki and Taylor who employed saline amnioinfusion for repetitive or prolonged variable decelerations. Results showed improvement of decelerations.[10]

Amnioinfusion is performed to restore the amniotic fluid volume, thereby cushioning the umbilical cord and thus correcting recurrent umbilical cord compressions, manifesting as variable decelerations, that lead to fetal acidemia (a condition predisposing to the meconium aspiration syndrome). It also serves to dilute thick meconium, thus reducing its mechanical and inflammatory effects (mechanical obstruction of the bronchioles and chemical pneumonitis). In turn, postpartum and neonatal infection rates decrease.[10]

A Cochrane systematic review on amnioinfusion for meconium-stained amniotic fluid has shown that amnioinfusion was associated with an overall reduction in the meconium aspiration syndrome and cesarean section rate.[12] However, previous trials included in this review had small sample sizes and their outcome measures were not clearly defined.[13,14] A clear benefit of amnioinfusion was seen in the largest study which was carried out in a setting where routine intrapartum fetal heart-rate monitoring and neonatal resuscitation were not available.[1]

A recent meta-analysis of 13 studies stratified those included according to clinical settings. In studies with standard peripartum surveillance, amnioinfusion is associated with reduction in cesarean section rates and improved perinatal outcome. However, in studies with limited peripartum surveillance, amnioinfusion was seen to improve perinatal outcome but has no measurable effect on cesarean section rates.[12] No local randomized studies on amnioinfusion have been made, although, based on anecdotes and experience, some Filipino obstetricians employ this method for relief of variable decelerations and dilution of meconium stained amniotic fluid. There is one locally published case report on the use of amnioinfusion for the treatment of severe variable decelerations.[17]

Amnioinfusion, however, is not without risk. Complications such as umbilical cord prolapse, amniotic fluid embolism and one case of iatrogenic polyhydramnios and elevated intra-uterine pressure during amnioinfusion, which led to fetal bradycardia, have been noted in literature.[14,15,16]

The greatest attraction of amnioinfusion is that it is relatively easy to perform, inexpensive and safe. Clinicians think that despite the subtle benefits of amnioinfusion, they have still adopted its use because the benefits seem to clearly outweigh the perceived risks to the mother and fetus.[1,8,9,10] There is a need to establish local data on amnioinfusion to encourage its uptake, given the strength of the various studies supporting its use during labor.

GENERAL OBJECTIVE

To assess the effect of amnioinfusion during labor with meconium stained amniotic fluid on mode of delivery

and maternal and perinatal outcomes.

SPECIFIC OBJECTIVES

1. To determine whether amnioinfusion reduces the rate of cesarean deliveries in patients with meconium stained amniotic fluid

2. To calculate the risk of meconium aspiration syndrome, NICU admission and perinatal death, as well as adverse maternal outcomes in patients who receive transcervical amnioinfusion for meconium stained amniotic fluid in labor

METHODS

This is a prospective randomized controlled trial carried out in the University of the Philippines-Philippine General Hospital Departmentof Obstetrics and Gynecology from June to September 2013. The study was approved by the University of the Philippines-Manila Research Ethics Board.

Two proportions power analysis was done for sample size determination in this study. (Please see Appendix E for the reference study)

The studypopulation consisted adult obstetric patients with term uncomplicated singleton pregnancies in cephalic presentation, with ruptured bag of waters and with evidence of meconium stained amniotic fluid. The patient should be between 2-6 cm cervical dilatation. Patients with a major medical illness, previous uterine incision other than low transverse, unless previous section was for cephalopelvic disproportion, urgent indication for delivery such as fetal distress or deteriorating maternal status, known fetal malformation and signs of a vertically transmissible infectious disease were excluded. Withdrawal from the study was done for patients with persistently increased uterine tone, any category III trace and a trace with recurrent variable decelerations.

Informed consent was taken from every participant. For every patient recruited into the study, the investigators completed an information data form and checklist documenting demographics, past medical and surgical history, labor characteristics, mode of delivery, indication for delivery, neonatal outcome, and presence of any neonatal or maternal morbidity.

Randomization was achieved thru a computer-generated randomization sampling technique.

Patients in the treatment group underwent the procedure immediately after randomization. Warmed 0.9 normal saline solution was used for infusion. A venoset was connected to the normal saline solution and flushed to avoid introducing air into the uterus.

Using sterile gloves, a vaginal examination was performed to evaluate for cord prolapse, establish dilatation and confirm presentation. A French 14 nasogastric tube was introduced through the cervix at a depth of 15 cm. After insertion, a bolus of 300 ml of warmed normal saline solution was infused over 1 hour.

Monitoring of maternal vital signs was performed hourly and as deemed necessary by the attending physician. A baseline cardiotocogram was performed prior to amnioinfusion. The patient was on continuous electronic fetal monitoring while undergoing the procedure. After amnioinfusion, another cardiotocogram was performed. This was repeated as often as deemed necessary by the attending obstetrician.

If the uterine tone is found to be persistently elevated, the infusion was discontinued and the uterine pressure allowed to equilibriate over five minutes. Resting uterine tone was reassessed. The infusion was discontinued if the new resting tone was 15 mm Hg above the baseline resting tone or 30 mm Hg maximum.

Patients in the control arm were afforded standard labor management.

STATISTICAL ANALYSIS

The study employed frequency and percent distribution in expressing categorical data. Meanwhile, mean, standard deviation and ranges were used as indicators of continuous data. To test differences of categorical data, Chi Square Test was utilized while for continuous data, independent t-test was used. An associated p-value lesser than 0.05 alpha was considered significant. The data was then processed using SPSS (Statistical Package for Social Sciences) version 18.

RESULTS

A total of 23 parturients underwent randomization, 11 to the amnioinfusion group and 12 to the no amnioinfusion group. There were no dropouts from the study.

The study groups are balanced with respect to sociodemographic characteristics, anthropometric variables and baseline obstetrical characteristics (Table 1). There was also no significant difference in the labor characteristics of both groups in terms of manner of amnion rupture, cervical dilatation at which the presence of meconium was detected and interval between detection of meconium and delivery (Table 2). Two patients in the control group experienced fetal tachycardia while being monitored during labor.

One of the primary outcomes, meconium aspiration syndrome, occurred in three infants on the no amnioinfusion group (25%) and in one infant in the amnioinfusion group (9%). There was no significant difference in these rates (Table 3).

Table 1. Demographics and Baseline Obstetric Characteristics

DEMOGRAPHICS	With Amnioinfusion (n = 11)		Without Amnioinfusion (n = 12)		p-value
Age					
19-25	7	64%	4	33%	0.146
26-30	3	27%	3	25%	0.901
31-35	1	9%	4	33%	0.159
36-40	0	0%	1	8%	0.328
41-45	0	0%	0	0%	1.000
Gestational Age in Weeks					
37-37 6/7	2	18%	2	17%	0.924
38-38 6/7	2	18%	2	17%	0.924
39-39 6/7	4	36%	1	8%	0.104
40-40 6/7	2	18%	4	33%	0.408
41-41 6/7	1	9%	2	17%	0.590
>/= 42	0	0%	1	8%	0.328
Number of Antenatal Visits					
none	0	0%	1	8%	0.328
1 - 5	7	64%	6	50%	0.510
6 - 10	5	45%	5	42%	0.855
>10	0	0%	0	0%	1.000
Body Mass Index (BMI)					
<18.9 (underweight)	0	0%	0	0%	1.000
18.9-23 (normal)	3	27%	3	25%	0.901
23.1-25 (overweight)	4	36%	4	33%	0.879
25.1-30 (obese I)	3	27%	5	42%	0.469
30.1-35 (obese II)	1	9%	0	0%	0.286
PAST MEDICAL HISTORY					
Medical History allergy to Amoxicillin	0	0%	1	8%	0.328
Previous Surgeries					
Status post oophorocystectomy for ovarian cyst	1	9%	0	0%	0.286
s/p primary LSCS for non-reassuring fetal status	0	0%	1	8%	0.328

There were no perinatal deaths in both groups. The rates of neonatal pneumonia and neonatal sepsis also did not differ significantly in both groups (0% in the amnioinfusion group versus 8% in the no amnioinfusion group and 9% in the amnioinfusion group versus 17% in the no amnioinfusion group, respectively) (Table 3).

One infant in the amnioinfusion group (9%) required intubation and was admitted to the Neonatal Intensive Care Unit. Three infants in the no amnioinfusion group (25%) were admitted to the Neonatal ICU. Two of these infants were intubated and one was on continuous positive airway pressure (Table 3).

The cesarean section rate did not differ significantly in both groups. One patient delivered by cesarean section for each of the two groups (9% for the no amnioinfusion group and 8% for the amnioinfusion group). The indications for cesarean section are chorioamniotis for the patient in the control group and fetal distress for the patient in the treatment arm (Table 4).

Table 2. Labor Characteristics

LABOR CHARACTERISTICS	With Amnioinfusion (n = 11)		Without Amnioinfusion (n = 12)		p-value
Induced	4	36%	2	17%	0.283
Spontaneous	7	64%	10	83%	0.283
Cervical dilatation when meconium was noted					
2-3 cms	2	18%	2	17%	0.924
4-5 cms	6	55%	2	17%	0.057
6 cms	3	27%	8	67%	0.059
Meconium detection to delivery interval					
0-3 hours	3	27%	8	67%	0.059
4-5 hours	4	36%	3	25%	0.554
6-9 hours	3	27%	1	8%	0.231
10-12 hours	1	9%	0	0%	0.286
>12 hours	0	0%	0	0%	1.000
Changes in FHR during amnioinfusion					
None	10	91%	10	83%	0.590
Others	0	0%	2	17%	0.156

Table 3. Neonal Morbidity

NEONATAL MORBIDITY	With Amnioinfusion (n = 11)		Without Amnioinfusion (n = 12)		p-value
Meconium aspiration syndrome	1	9%	3	25%	0.315
Neonatal Pneumonia	0	0%	1	8%	0.328
Neonatal Sepsis	1	9%	2	17%	0.590
Perinatal death	0	0%	0	0%	1.000
NICU Admission					
DRI (directly roomed in)	10	91%	9		
NICU 2 (Neonatal ICU, non oxygen-requiring)	0	0%	0	75% 0%	0.315 1.000
NICU 3 (Neonatal ICU, oxygen-requiring)	1	9%	3	25%	0.315

The neonatal outcome in terms of pediatric aging, weight at delivery, weight for gestational age as well as APGAR score at 1 and 5 minutes also had no significant difference between the infants of mothers in the control and treatment arms (Table 5).

Maternal pyrexia, described as a temperature above 38 degrees Celsius, was seen more in the no amnioinfusion group. Two patients in this group (17%) had a temperature range of 38-38.9 degrees Celsius during their admission, excluding the first 24 hours from delivery. Hospital admission was also longer for patients in the no amnioinfusion group with seven patients (58%) in the amnioinfusion group admitted for 4-7 days as opposed to the three patients (27%) in the amnioinfusion group (Table 6).

Table 4. Mode of Delivery and Indications of Delivery

MODE OF DELIVERY					
Cesarean section	1	9%	1	8%	0.949
Spontaneous vaginal	9	82%	10	83%	0.924
Forceps delivery	1	9%	1	8%	0.949
INDICATION OF DELIVERY					
Fetal distress	1	9%	0	0%	0.286
Dystocia	0	0%	0	0%	1.000
Deteriorating maternal status	0	0%	0	0%	1.000
Chorioamnionitis	0	0%	1	8%	0.328
Others (specify)	0	0%	0	0%	1.000
Poor maternal effort	1	9%	1	8%	0.949

Table 5. Neonatal Outcome

Neonatal Outcome	**With Amnioinfusion (n = 11)**		**Without Amnioinfusion (n = 12)**		**p-value**
Sex					
Male	5	45%	5	42%	0.855
Female	6	55%	7	58%	0.855
Pediatric aging					
37 weeks	1	9%	1	8%	0.949
38 weeks	0	0%	2	17%	0.156
39 weeks	7	64%	5	42%	0.292
40 weeks	3	27%	2	17%	0.538
41 weeks	0	0%	2	17%	0.156
42 weeks	0	0%	0	0%	1.000
Weight at delivery					
2000-2499 grams	1	9%	1	8%	0.949
2500-2999 grams	3	27%	5	42%	0.469
3000-3499 grams	6	55%	6	50%	0.827
3500-3999 grams	1	9%	0	0%	0.286
>/= 4000 grams	0	0%	0	0%	1.000
APGAR score					
1 minute					
3	1	9%	1	8%	0.949
9	10	91%	11	92%	0.949
5 minutes					
7	1	9%	0	0%	0.286
9	10	91%	12	100%	0.286
Weight-for-gestational-age					
SGA (small for gestational age)	0	0%	0	0%	1.000
AGA (appropriate for gestational age)	11	100%	12	100%	1.000
LGA (large for gestational age)	0	0%	0	0%	1.000

Table 6. Maternal Morbidity

MATERNAL MORBIDITY					
Maternal Pyrexia					
36-36.9 deg Celsius	7	64%	7	7	0.795
37-37.9 deg Celsius	4	36%	3	3	0.554
38-38.9 deg Celsius	0	0%	2	2	0.156
39-39.9 deg Celsius	0	0%	0	0	1.000
Length of maternal hospital stay					
1 day	0	0%	0	0	1.000
2-3 days	8	73%	5	5	0.133
4-7 days	3	27%	7	7	0.133
8-14 days	0	0%	0	0	1.000
>14 days	0	0%	0	0	1.000

DISCUSSION

Amnioinfusion during labor for meconium stained amniotic fluid has been proposed as a rational approach to prevent and manage problems arising from the infant's passage of meconium. It has been shown to play a role in decreasing the rate of operative intervention as well as decreasing the incidence of meconium aspiration syndrome. Studies on amnioinfusion for meconium stained amniotic fluid in labor have shown conflicting results. Fraser and colleagues, in a multicenter randomized trial, concluded that amnioinfusion should not be recommended for patients with meconium stained amniotic fluid in centers with standard peripartum surveillance.[21] However, Hofmeyr, also in a multicenter randomized controlled trial, found that amnioinfusion effected reductions in cesarean section rate, meconium aspiration syndrome and perinatal mortality.[1] In our study, there was note of a decrease in rates of meconium aspiration syndrome and neonatal intensive care unit admission among the babies of mothers who underwent amnioinfusion. There was also a lower number of babies with neonatal pneumonia and sepsis. Previous reports have shown that amnioinfusion indeed reduces these occurences by diluting thick meconium, reducing the risk for aspiration and subsequent fetal distress. This in turn reduces the burden of complications in centers such as ours.

There have been reports of a 35%-55% decrease in the caesarean section rate following amnioinfusion.[10,22,23] The CRAMP study[1], on the other hand, shows improved perinatal outcomes from amnioinfusion but this did not report any effect on cesarean section rates. Our study found no difference in cesarean section rates and is consistent with those of other studies abroad.[24,25,26]

In our study, there was also noted difference in the rates of meconium aspiration syndrome, neonatal intensive care unit admission and APGAR scores. Previous reports have shown that amnioinfusion reduces these occurrences by diluting thick meconium, thus reducing the burden of complications in developing countries where neonatal intensive surveillance facilities are scarce and often expensive, like ours.[1,25,26]

Maternal outcome postpartum was similar in the two groups in terms of fever and duration of hospital stay. Although the difference is not statistically significant, there were more patients with postpartum fever in the control group. The decrease in incidence of puerperal pyrexia in the treatment arm could be due to the diluting effect of amnioinfusion on bacteria that enter the uterus.[27] Results in the Hofmeyr study are similar.[12] Maternal hospital stay is also seen to be longer in mothers in the control group, perhaps owing to the continued surveillance necessary following their febrile morbidities.

CONCLUSION

Amnioinfusion is a relatively simple technique of reducing perinatal and maternal morbidity in patients with meconium stained amniotic fluid. Although this study did not show any significant difference between the two groups, there is a trend towards better neonatal outcomes and decreased maternal morbidity with amnioinfusion.

REFERENCES

1. Mahomed K, Mulambo T, Woelk G, Hofmeyr GJ, Gülmezoğlu AM. The Collaborative Randomized Amnioinfusion for Meconium Project (CRAMP), II: Zimbabwe. *Br J Obstet Gynaecol* 1998;105:309-13.

2. Katz VL, Bowes WA. Meconium aspiration syndrome: reflections on a murky subject. *Am J Obstet Gynecol* 1992;166:171-183.

3. Dargaville, P. A.; Copnell, B.; Australian and New Zealand Neonatal Network (2006). "The Epidemiology of Meconium Aspiration Syndrome: Incidence, Risk Factors, Therapies, and Outcome". Pediatrics 117 (5): 1712.

4. Davis RO, Philips JB, Harris BA, Wilson ER, Huddleston JF. Fetal meconium aspiration syndrome occurring despite airway management considered appropriate. *Am J Obstet Gynecol* 1985;151:731-736.

5. Richey SD, Ramin SM, Bawson RE, et al. Markers of acute and chronic asphyxia in infants with meconium-stained amniotic fluid. *Am J Obstet Gynecol* 1995;172:1212-5.

6. Vain NE, Szyld EG, Prudent LM, Wiswell TE, Aguilar AM, Vivas NI. Oropharyngeal and nasopharyngeal suctioning of meconium stained neonates before delivery of their shoulders: multicenter, randomized controlled trial. *Lancet* 2004;364:597-602.

7. Wiswell TE, Gannon CM, Jacob J, Goldsmith L, Szyld E, Weiss K, et al. Delivery room management of the apparently vigorous meconium-stained neonates: results of the multicenter, international collaborative trial. *Pediatrics* 2000;105:1-7.

8. Malhotra B, Agarwal N. Amnioinfusion: current status. *Asian J Obstet Gynaecol Pract* 2002;6:12-6.

9. Gabbe SG, Ettinger BB, Freeman RK, Martin CB. Umbilical cord compression associated with amniotomy: laboratory observations. *Am J Obstet Gynecol*. 1976;126:353-5.

10. Miyazaki FS, Taylor NA. Saline amnioinfusion for relief of variable or prolonged decelerations. A preliminary report. *Am J Obstet Gynecol*. 1983;146:670-8.

11. Choudhary D, Bano I, Ali SM. Does amnioinfusion reduce caesarean section rate in meconium-stained amniotic fluid. *Arch Gynecol Obstet* 2010;282:17-22

12. Hofmeyr GJ. Amnioinfusion for meconium- stained liquor in labor. *Cochrane Database Syst Rev* 2002;1:CD000014.

13. Pierce J, Gaudier FL, Sanchez-Ramos L. Intrapartum amnioinfusion for meconiumstained fluid: meta-analysis of prospective clinical trials. *Obstet Gynecol* 2000;95:1051-6.

14. Wenstrom K, Andrews WW, Maher JE. Amnioinfusion survey: prevalence, protocols, and complications. *Obstet Gynecol* 1995;86:572-6.

15. Dragich DA, Ross AF, Chestnut DH, Wenstrom K. Respiratory failure associated with amnioinfusion during labor. *Anesth Analg* 1991;72:549-51.

16. Maher JE, Wenstrom KD, Hauth JC, Meis PJ. Amniotic fluid embolism after saline amnioinfusion: two cases and review of the literature. *Obstet Gynecol* 1994;83:851-4.

17. Villacarlos MG. Amnioinfusion in the treatment of severe variable decelerations: A case report. *Philippine Scientific Journal* 1998;31(3):60-64.

18. Poggi SH, Ghidini A. Pathophysiology of meconium passage into the amniotic fluid. *Early Human Development* 2009;85:607-610.

19. G. M. Cleary and T. E. Wiswell, "Meconium-stained amniotic fluid and the meconium aspiration syndrome: an update," *Pediatric Clinics of North America* 1998;45(3):511-529.

20. Rubin BK, Tomkiewicz RP, Patrinos ME, Easa D. The surface and transport properties of meconium and reconstituted meconium solutions. *Pediatr Res* 1996;40:834-8.

21. Fraser WD, et al. Amnioinfusion for the Prevention of the Meconium Aspiration Syndrome. *New England Journal of Medicine September* 2005; 353(9): 909-917.

22. Macri CJ, Schrimmer DB. Prophylactic amnioinfusion improves outcome of pregnancy complicated by thick meconium and oligohydramnios. *Am J Obstet Gynecol* 1992; 167:117-121.

23. Puertas A, Paz Carrillo M, Molto L, Alvarez M, Sedeno S, Miranda JA. Meconium-stained amniotic fluid in labor: a randomized trial of prophylactic amniofusion. *Eur J Obstet Gynecol Reprod Bio 1* 2001; 99:33-37.

24. Sadovsky Y, Amon E, Bade ME, Petrie RH (1989) Prophylactic amnioinfusion during labour complicated by meconium; a preliminary report. *Am J Obstet Gynecol* 161:613-617.

25. Cialone PR, Sherer DM, Ryan RM, Sinkin RA, Abramowicz J (1994) Amnioinfusion during labour complicated by particulate meconium-stained amniotic fluid decreases neonatal morbidity. *Am J Obstet Gynecol* 170:842-849.

26. Sponge CY, Ogundipe OA, Ross MG (1994) Prophylactic amnioinfusion for meconium-stained amniotic Xuid. *Am J Obstet Gynecol* 171:931-935.

27. Moen MD, Richard E, Paul G, Susan G. Effect of amnioinfusion on the incidence of postpartum endometritis in patients undergoing caesarean delivery. *J Reprod Med* 1995;40:383-386.