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Association of Meconium-Stained Amniotic Fluid With Umbilical Cord Arterial Blood Gas Parameters and Apgar Score: A Brief Report

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Abstract

Objectives: Meconium-stained amniotic fluid (MSAF) increases the risk of morbidity and mortality of neonates. Meconium aspiration syndrome (MAS) can end in hypoxemia, hypercarbia, and acidosis. The aim of this study was to compare the results of umbilical cord arterial blood gas (ABG) analysis and Apgar score of the neonates with and without MSAF.

Materials and Methods: Of all women (N=2037) who gave birth by caesarean section at Shohadaye-Tajrish hospital from 2015 to 2018, 100 women with MSAF were considered as the case group and 100 with normal amniotic fluid as the control group. The gestational age (GA) at caesarean delivery, neonate's gender, 1 and 5 minutes Apgar scores (AS), and results of umbilical cord ABG analysis were compared between the groups using chi-square and t test. Statistical analysis was performed using SPSS version 24.0.

Results: The case group had a higher mean GA (39.19±1.52 weeks vs. 38.57±0.671; $P<0.001$) and the control group had a higher mean 1-minute AS (9.58±0.25 vs. 8.47±0.327; $P<0.001$), while the distribution of the neonate's gender and frequency of low/normal 5-minute AS were not different between the groups ($P>0.05$). The control group had a higher mean pressure of oxygen (32.44±24.89 vs. 25.83±16.63; $P=0.029$); other parameters were not different between the two groups ($P>0.05$).

Conclusions: The lower pressure of oxygen in neonates with MSAF, despite no difference in acidosis suggest that various factors have to be considered in order to differentiate pathologic and physiologic MSAF.

Keywords: Meconium, Meconium aspiration syndrome, Amniotic fluid, Blood gas analysis, Umbilical cord

Introduction

Meconium is a thick germ-free material which is first recognized in the fetal intestine around 12 weeks of gestation and stores in the fetal colon throughout gestation (1). Early passage to the amniotic fluid causes meconium-stained amniotic fluid (MSAF) (1). MSAF happens in about 7-20% of neonates, more commonly in advanced maternal age, advanced gestational age (GA), and cesarean section (C/S) deliveries (2), as well as cases with a longer duration of labor (3). Some suggest MSAF as a symptom during term pregnancy (4) and recommend that neonates with normal appearance, pulse, grimace, activity, and respiration (Apgar) score (AS) can be discharged from the hospital (5).

The presence and accumulation of the meconium, including debris, desquamated cells, gastrointestinal secretions, and lanugo hair, in the sterile amniotic fluid can cause intra-amniotic infection and inflammation, as well as acute placental inflammation (6,7). More importantly, aspiration of the meconium by the neonate, during ante- or intra-partum period, can cause meconium aspiration syndrome (MAS), airway obstruction, and asphyxia in neonates (8), while MSAF is also associated with higher neonatal morbidity, independent of MAS (9,10).

The viscosity and degree of meconium staining are considered fundamental issues concerning MAS, as thick meconium causes mechanical obstruction, resulting in atelectasis and reduced arterial oxygen pressure (PaO_2) or air leaks and increased partial pressure of arterial carbon dioxide ($PaCO_2$) in cases with incomplete MAS, both of which end in hypoxemia, hypercarbia, acidosis, and finally persistent pulmonary hypertension (11, 12).

According to the mechanism of MAS, some have suggested using umbilical cord arterial blood gas analysis, as low pH has been associated with higher rates and severe grades of MSAF (13), as well as low AS and adverse neonatal outcome (14,15). The aim of this study was to compare the results of umbilical cord ABG analysis and Apgar score of the neonates with and without MSAF.

Materials and Methods

Study Design

In this study, all women who gave birth by C/S at Shohadaye-Tajrish hospital from March 21, 2015, to

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March 22, 2018 (three years) were selected as the study population, making a total of 2037 pregnant women. Of these women, 155 cases with MSAF were selected as the case group and 100 women with clear (without meconium-stained) amniotic fluid were selected as the control group. The individuals in the control group were selected randomly from the study population and matched with the case group. The subjects in the case group were included in the study by census method. Women with incomplete medical records were excluded from the study before the statistical analysis. In the control group, such cases were replaced with another woman with complete medical records.

The following information was recorded from the hospital's medical records for both groups: GA at C/S delivery, neonate's gender, 1 and 5 min AS of the neonate, and the results of umbilical cord ABG analysis (including hydrogen [pH], partial pressure of carbon dioxide [PCO_2], partial pressure of oxygen [PO_2], bicarbonate [HCO_3], oxygen saturation [O_2Sat], and base excess [BE].

According to the hospital's protocol, after birth, a 10-20 cm umbilical cord was separated by two clamps, one close to the neonate and the other close to the placenta; the arterial blood sample was then taken by a 2-mm plastic heparinized syringe. The syringe was recapped; the samples were kept at room temperature for a maximum of 60 minutes and sent to the laboratory.

Statistical Analysis

Apgar score of the first minute was reported as mean ± standard deviation (SD) and a fifth minute Apgar score of ≤7 was considered as abnormal and >7 as normal. pH of the umbilical cord blood was categorized into four groups: <7 as very low, 7-7.2 as low, 7.2-7.25 as borderline, and >7.25 as normal. PCO_2 was categorized into two groups of ≤54 and >54 and BE was categorized into three groups: ≤-12 as severe base deficit, values between -10 and -12 as base deficit, and >-10 as normal. The frequency of the categories was recorded and the comparison of the categorical variables was performed using chi-square test. The quantitative variables were compared between the two groups using *t* test. IBM SPSS version 24.0 (NY: IBM Corp) was used for statistical analyses and *P* values of 0.05 or less were considered statistically significant.

Results

The data of a total of 200 women were analyzed; 100 in the case group (MSAF) and 100 in the case group (clear amniotic fluid). The distribution of neonate's gender, GA, mean AS at 1 minute, and frequency of low/normal AS at 5 minutes were shown in Table 1. As it was demonstrated, the case group had a higher mean GA ($P<0.001$), while the distribution of the neonate's gender was not different between the groups ($P>0.05$). Moreover, the control group had a higher mean AS at the first minute ($P<0.001$), while the frequency of low/normal AS at 5 minutes was not different between the two study groups ($P>0.05$).

The comparison of the results of umbilical cord arterial blood gas analysis between the two study groups showed that the control group had a higher mean PO_2 ($P=0.029$); however, the other parameters were not different between the two study groups ($P>0.05$; Table 2).

Discussion

In the present study, the results of the comparison of the 1 and 5 minutes AS between the case and control groups with and without MSAF showed that the control group had a higher mean AS at 1 minute, but no difference was observed between the groups at 5 minutes. These results indicate that MSAF is not necessarily associated with adverse neonatal outcomes, which is of great significance, as considering MSAF as an adverse pathologic event can result in unnecessary hospitalization of the neonate that increases the medical costs and risk of nosocomial infection in the neonate (16). Comparing these results with those of previous studies shows a great discrepancy; nonetheless, it is of great importance to know whether we should consider MSAF as a pathologic condition or a physiologic phenomenon. A number of studies have recommended MSAF as a common symptom during term pregnancy (4) that is consistent with the general results of our study. In the study by Mundhra and Agarwal, the comparison of the two groups with and without MSAF showed a higher rate of fetal bradycardia, spontaneous vaginal delivery, C/S deliveries, lower 1 minute AS, birth asphyxia, and NICU admission, but no difference was observed in 5 minutes AS (17). This finding is similar to the results of our study, considering AS; however, we

Table 1. Comparing the Neonates' Gender, Gestational Age, and Apgar Scores in Two Study Groups

		Case Group (n=100)	Control Group (n=100)	*P* Value
Neonate's gender, No (%)	Male	53 (50.5)	52 (49.5)	0.887[a]
	Female	47 (49.5)	48 (50.5)	
Gestational age, mean ±SD		39.19±1.52	38.57±0.67	<0.001[b]
1-minute Apgar score, mean ±SD		8.47±0.32	9.58±0.25	<0.001[b]
5-minute Apgar score, No.(%)	≤7	1 (100)	0	0.316[a]
	>7	99 (49.7)	100 (50.3)	

[a] The results of Chi-square test, [b] The results of independent samples *t* test.

Table 2. Comparing the Results of Umbilical Cord Arterial Blood Gas Analysis Between the Two Study Groups

		Case Group (n=100)	Control Group (n=100)	*P* Value
pH (mmol/L), No.(%)	<7	1 (100)	0	0.410[a]
	7-7.2	17 (60.7)	11 (39.3)	
	7.2-7.25	13 (43.3)	17 (56.7)	
	≥7.25	69 (48.9)	72 (51.1)	
PCO_2 (mm Hg), No.(%)	≥54	24 (51.1)	23 (48.9)	0.868[a]
	<54	76 (49.7)	77 (50.3)	
BE (mEq/L), No.(%)	≤-12	12 (70.6)	5 (29.4)	0.205[a]
	-10 to -12	5 (50)	5 (50)	
	>-10	83 (48)	90 (52)	
pH (mmol/L), mean ±SD		7.28±0.10	7.29±0.08	0.448[b]
PCO_2 (mm Hg), mean ±SD		47.59±12.55	47.26±13.99	0.861[b]
HCO_3 (mEq/L), mean ±SD		22.02±5.17	22.17±4.78	0.834[b]
PO_2 (mm Hg), mean ±SD		25.83±16.63	32.44±24.89	0.029[b]
O_2Sat (%), mean ±SD		36.28±23.67	43.13±26.01	0.053[†]
BE (mEq/L), mean ±SD		-4.78±5.70	-4.59±4.44	0.801[b]

PCO_2: partial pressure of carbon dioxide, BE: base excess, HCO3: Bicarbonate, PO_2: partial pressure of oxygen, O_2Sat: oxygen saturation.
[a] The results of chi-square test, [b] The results of independent samples *t* test; all tests were considered significant at *P* values < 0.05

did not evaluate the clinical outcome of the neonates. Other studies have also shown that neonates with MSAF (5 minutes AS of >8) have a very low risk of MAS in uncomplicated pregnancy and are thus suggested to be discharged from the hospital (5,18). Another study investigating factors associated with low 1 minute AS (<7) have considered MSAF as a significant predictor (19), although the study design differed. On the contrary, some previous reports indicated a low AS and high risk of asphyxia and MAS in neonates with MSAF (20-22), but these studies had some limitations. For instance, the study by Vaghela et al has only considered the outcomes in neonates with MSAF, without comparison with a control group (20), Mohammad et al have not mentioned the time of AS (21), and Shaikh et al have not reported the *P* values. On the other hand, some others report MSAF as an important risk factor for adverse neonatal outcomes with strong proof (9,23-25), which is inconsistent with the results of the present study. These discrepancies in the results of the studies can be attributed to the difference in meconium viscosity, as well as the confounding effect of mode of delivery, pregnancy complications, and neonatal congenital abnormalities/defects on the results that have not been considered in the studies. Due to the significance of the effect of MSAF on AS, further studies are required in this regard to draw a definite conclusion.

Another important variable studied was the results of the umbilical cord ABG analysis. It was shown that neither frequency of categories, nor mean values of pH, BE, HCO_3 differed between the case and control groups. Although PO_2 was lower in the case group, no significant difference was observed between the groups in terms of O_2Sat or PCO_2. These results indicate that MSAF is not associated with acidosis, hypoxemia, and hypercarbia. Moreover, no association was found between different degrees of MSAF and low pH of arterial cord blood, as according to the results of their study, 85.7% of grade I, 68.9% of grade II, and 59.4% of grade III MSAF had pH >7.2 (15). The results of this study confirmed those of our study, considering the rejection of the association of acidosis with MSAF; although they had no control group. The results of case-control studies have also shown that cord blood pH, BE, and neonatal metabolic acidosis were not different between neonates with and without MSAF (26,27), which confirms the results of the present study. On the contrary, other researchers have suggested MSAF as the first risk factor of abnormal results of umbilical cord ABG analysis (28), while we did not observe any significant difference between the case and control groups. Studying the venous blood gas results showed that all parameters, including pH, PCO_2, HCO_3, O_2Sat, and base deficit were different between neonates born with MSAF and controls, while PO_2 was not different (29), which is completely opposite to the results of the present study. The umbilical cord blood pH is considered an important predictor of MAS, asphyxia, and other adverse neonatal outcomes (30-32) and is thus suggested as an accessible objective assessment tool (28). Nonetheless, there is insufficient evidence considering the association of ABG parameters with MSAF, and more studies are required in this regard.

Another significant finding of our study was the higher mean GA of the neonates with MSAF, compared to the control group, which confirms the results of previous studies, suggesting a higher risk of MSAF by advanced GA (10,33,34). It has also been suggested that the risk of MAS and other adverse neonatal outcomes is higher in advanced GAs (35). Therefore, greater attention should be paid to term and post-term deliveries considering MSAF.

One of the limitations of the present study was the retrospective analysis of the results, which limited the

evaluation of some variables which were not recorded in the medical records, such as meconium viscosities. Therefore, we have included both thin and thick meconium, which can affect the results. Furthermore, we could not investigate the causal relationship between the variables because of the nature of the study and we had no follow-up. Another limitation of our study was that we have only included C/S deliveries from referrals to one medical center; therefore, the results cannot be generalized to the whole population.

Conclusions

In conclusion, the results of our study showed that MSAF does not increase the risk of hypercarbia, acidosis, or base deficit, while, it can reduce PO_2. These results suggest that various factors have to be considered in order to differentiate pathologic and physiologic MSAF.

Considering these controversial results and discrepancy of the results of previous studies, we conclude that several confounders may play a role in the association of MSAF with acidosis; therefore, future randomized clinical trials with large sample size and follow-up are required to determine the exact role of MSAF in the neonate's outcome.

Authors' Contribution

Study concept and design: BN and MA, drafting: PP and MA and FN, Statistical Analysis: FN and PP.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

Written informed consent was obtained from the participants. The protocol of the study was approved by the Research Ethics Committee of Shahid Beheshti University of Medical Sciences (SBMU)..

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