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Evaluation of gastric aspirate shake test in predicting surfactant need in preterm infants with neonatal respiratory distress syndrome: a cross-sectional study

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Keypoints

Gastric aspirate shake test (GAST) can be used as a suitable tool in predicting the need for surfactant in preterm infants.

Abstract

Introduction

Neonatal respiratory distress syndrome (NRDS) is one of the most common respiratory diseases in preterm infants. Evaluation tests have a major role in determining the need for surfactant in preterm infants. Therefore, this study aimed to investigate the effect of gastric aspirate shake test (GAST) on predicting surfactant need in infants. This prospective, cross-sectional study was performed on 91 infants with gestational age less than 34 weeks in the neonatal unit of a teaching hospital in Zabol, southern Iran, from 1 February 2019 to 30 July 2019. The infants were selected through convenient sampling. The sampling method used was easy and data were collected using an oral interview with pregnant mothers and through the examination of records and completion of questionnaire. Data were analyzed by using SPSS v21 and descriptive statistics and regression test were used for odds ratio.

Materials and methods

This prospective, cross-sectional study was performed on 91 infants with gestational age less than 34 weeks in the neonatal unit of a teaching hospital in Zabol, southern Iran, from 1 February 2019 to 30 July 2019. The infants were selected through convenient sampling. The sampling method used was easy and data were collected using an oral interview with pregnant mothers and through the examination of records and completion of questionnaire. Data were analyzed by using SPSS v21 and descriptive statistics and regression test were used for odds ratio.

Results

91 infants were included in this study, 62 were male (68.1%) and 29 (31.9%) were female. The mean birth weight of infants was 1662 ± 593 g and their mean age was 31.7 ± 2.5 weeks. The sensitivity, specificity, negative predictive value, and positive predictive value in the gastric aspirate shake test (GAST) were 100%, 40.7%, 100%, and 48.6%, respectively. According to the present study, there was no significant relationship between the type of delivery and hyaline membrane disease ($P > 0.05$).

Conclusion

Our study showed that the children of mothers with hypertension, addiction, and diabetes were less likely than others to have hyaline membrane disease and need surfactant administration.

The administration of corticosteroid drugs to mothers is also associated with the occurrence of hyaline membrane disease.

Keywords

Hyaline Membrane Disease, Gastric Aspirate Shake Test, Surfactant, Preterm Infant

Introduction

Neonatal respiratory distress syndrome (NRDS) is one of the most common respiratory diseases and the leading cause of mortality, morbidity and hospitalization in preterm infants, so that 24% of neonatal deaths are due to NRDS [1]. It is also a long-term respiratory problem among infants who survive [2]. NRDS is also called infant respiratory distress syndrome and hyaline membrane disease [3]. The main cause of NRDS is surfactant deficiency and clinical symptoms include tachypnea, cyanosis, granting, and increased oxygen demand. These symptoms usually start at birth, but in newborns, especially older preterm infants, may not be diagnosed until several hours after birth [4]. Diagnosis is usually based on clinical findings and chest radiography. The main treatment is surfactant replacement therapy (SRT), leading to better clinical improvement in neonates [5]. There are generally two ways to administer surfactants, 1) prophylactic and 2) rescue [5].

In the prophylaxis method, surfactant is administered to all infants who are at high risk for NRDS (such as infants less than 30 weeks gestational age) immediately after birth before the onset of clinical symptoms and usually in the delivery room. But in the rescue method, surfactant is administered after the onset of clinical symptoms and diagnosis of NRDS [6]. Today, prophylaxis method is not very welcomed, despite the reduction in mortality and pneumothorax, as some infants may eventually not require surfactant and in addition to the high costs associated with surfactant administration, infants unduly exposed to intubation- and ventilator-induced lung injuries for surfactant administration [7-9]. Therefore, treatment or rescue is preferred in most centers of the world. In this method, although surfactants are administered after the onset of clinical symptoms, various studies suggest that surfactants should be administered as soon as possible after NRDS diagnosis, resulting in reduced mortality, reduced chronic lung diseases, reduced pneumothorax, reduced hospitalization costs, reduced hospital stay, and outcome improvement in infants [12-12]. It has been shown that even reducing the injection time from three hours to two hours after birth can significantly reduce the mortality and complication caused by hyaline membrane disease (HMD) by up to 16% [13, 14]. Since HMD is a progressive disease that may have mild clinical symptoms in the early hours and it may take several hours for the significant clinical symptoms to appear and the patient develops pulmonary failure and requires intubation, therefore, we will lose the golden opportunity to administer the surfactant in the first two hours after birth. Thus, a major diagnostic and therapeutic challenge is to identify neonates with NRDS diagnosis who will need surfactant treatment in the coming hours after birth. For this reason, a method that can predict the need for surfactants in neonates, while confirming the diagnosis of surfactant deficiency in patients with clinical symptoms of NRDS, is very helpful in the treatment of these patients [15].

Gastric aspirate shake test (GAST) is one of the clinical ways in which these at-risk infants can be diagnosed quickly after birth [15]. This test is very easy, inexpensive, and can be performed at the patient's bedside. In short, the way to do this test is to mix half a milliliter of gastric secretions prepared in the first half hour after birth with half a milliliter of normal saline and one milliliter of 95% alcohol in a tube and shake the contents of the tube. The test is interpreted as the formation or non-formation of bubbles at the liquid and air levels. Lack of bubble formation (negative test) indicates surfactant deficiency and bubble formation only in the tube medium (intermediate test) and formation of bubbles at the entire surface of the liquid and air (positive test) indicate lung maturity and adequate surfactant [15, 16]. The purpose of this study was to investigate the effect of gastric aspirate shake test on predicting the need for surfactant in infants.

Materials and methods

This prospective, cross-sectional study was performed on 91 infants with gestational age less than 34 weeks in the neonatal unit of a teaching hospital in XXXX, southern XXXX, from 1 February 2019 to 30 July 2019. The infants were selected through convenient sampling. Inclusion criteria were gestational age less than 34 weeks, respiratory distress score above 5, and having HMD. Exclusion criteria included presence of congenital anomalies (diaphragmatic hernia, pulmonary agenesis, congenital cystic adenomatoid malformation, lung bronchogenic cyst, upper respiratory tract anomalies, esophageal atresia, congenital heart anomalies, and brain anomalies such as hydrocephalus), severe asphyxia (neonates with fetal acidosis pH < 7, 5-minute Apgar score of 0–3, hypoxic-ischemic encephalopathy (decrease in consciousness, changes in tone and seizure), and having meconium aspiration, pneumonia and pneumothorax.

In order for collecting data, the gastric aspirate shake test (GAST) was first performed within the first half hour after birth as follows: In the first half hour after birth, gastric secretions were aspirated by insertion of a gastrostomy tube before the first feeding. Gastric secretions indicated pulmonary secretions and amniotic fluid within the first half hour after birth and then mixed with it. 0.5 ml of these gastric secretions was then transferred into a clean glass tube and 0.5 ml of normal saline was drawn off using another syringe and added to the tube. The tube was covered with a plastic cap or parafilm and its contents -a total of one milliliter –were shaken well for 15 seconds. The tube cap was then removed and 1 ml of 95 °C alcohol was drawn off using a third syringe and added to the tube. Now, the contents of the tube are 2 ml. The tube cap was reinserted and its contents were well shaken again for 15 seconds. Then the tube was placed in an upright position for 15 minutes and the liquid surface was examined for the result of the test as follows: If there is no air bubble on the surface, the test result will be negative, indicating the lack of surfactant or surfactant deficiency. If the air bubbles are just around the tube, but do not cover the entire surface, the test result will be intermediate, indicating that there are small amounts of surfactant, although not adequate. If the whole surface is covered with air bubbles, the test result will be positive, indicating adequate amounts of surfactant or surfactant adequacy [13]. If the test result is negative or intermediate (the test shows surfactant deficiency), the result will be false positive (FP); and if the test result is positive (the test does not show surfactant deficiency), the result will be true negative (TN). While, for those patients whose test result is negative or moderate (the test shows surfactant deficiency) and they eventually need surfactant, the result is true positive (TP). And also, for those patients whose test result is positive (the test does not show surfactant deficiency) but eventually need surfactants, the result is false negative (FN). The sensitivity, specificity, positive predictive value, and negative predictive value were calculated using the following formulas:

$$\text{Sensitivity: } \frac{TP\times 100}{Tp+FN},$$

$$\text{Specificity: } \frac{TN\times 100}{TN+FP},$$

$$\text{Positive predictive value: } \frac{TP\times 100}{Tp+FP},$$

$$\text{Negative predictive value: } \frac{TN\times 100}{TN+FN}$$

After data collection, data were analyzed using SPSS v21.

Results

In this study, the gastric aspirate shake test (GAST) was evaluated to predict the need for surfactant in infants with hyaline membrane disease (HMD), gestational age less than or equal to 34 weeks, and respiratory distress score greater than or equal to 5. In this study, 91 infants were enrolled, 62 (68.1%) were male and 29 (31.9%) were female. The average birth weight of infants was 1662g and their standard deviation was 593g. The lowest and highest birth weights were 540 and 3200 g, respectively. Their mean gestational age was 31.7 weeks and their standard deviation was 2.5. The minimum and maximum age were 26 and 34 weeks, respectively. Normal delivery and cesarean delivery rates were 38.5% (35 cases) and 61.5% (56 cases), respectively. Results of the gastric aspirate shake test showed that 49.5% (45 infants) had negative response, 9.9% (9 infants) had intermediate response, and 40.6% (37 infants) had positive response. The frequency of newborn preterm infants with hyaline membrane disease or respiratory distress syndrome requiring surfactant injection was 51 (54%), and 40 (44%) infants did not receive surfactant.

66.6% (6 infants) whose test result was intermediate received surfactant and no surfactant was administered and injected to the remaining 33.4% (3 infants). Surfactant was also administered to 45 (100%) infants whose test result was negative.

In our study, in terms of the history of disease and addiction, mothers of patients treated had a prevalence of 7.7% (7 patients) and 16.5% (15 patients) in diabetes and hypertension, respectively. The frequency of mothers with a history of addiction was also 19.8% (18 patients). The odds ratio for diabetes risk factor was 0.199. This means that the presence of diabetes in the mother reduced the risk of receiving surfactant 0.199 times, which was statistically significant (P = 0.01). 16 (17.6%) infants had positive maternal diabetes, 4 (7.8%) infants received surfactant, and 12 (30%) infants did not receive surfactant.

The odds ratio for hypertension risk factor was 0.33. This means that the presence of hypertension in the mother reduced the risk of receiving surfactant 0.33 times, which was statistically significant (P = 0.036) .20 (22%) infants had positive maternal hypertension, 7 (13.7%) infants received surfactant, and 13 (32.5%) infants did not receive surfactant.

The odds ratio for addiction risk factor was 0.311. This means that the presence of addiction in the mother reduced the risk of receiving surfactant 0.311 times, which was statistically significant (P = 0.035). 18 (19.8%) infants had positive maternal addiction, 6 (11.8%) infants received surfactant, and 12 (30%) infants did not receive surfactant.

The odds ratio for corticosteroid administration was 0.378. This means that the administration of corticosteroids to the mother reduced the risk of receiving surfactant 0.378 times, which was statistically significant (P = 0.03).The odds ratio for gender risk factor was 2.8. This means that male gender increased the risk of receiving surfactant 2.8 times, which was statistically significant (P = 0.03).

The odds ratio for the type of delivery risk factor was 1.072. This means that the type of delivery increased the risk of receiving surfactant 1.072 times, which was not statistically significant (P = 0.3).

The sensitivity, specificity, negative predictive value, and positive predictive value in the GAST were 100%, 40.7%, 100% and 48.6%, respectively.

Discussion

In the present study aimed at determining the effect of gastric aspirate shake test (GAST) on predicting the need for surfactant in infants with gestational age less than or equal to 34 weeks with hyaline membrane disease (HMD) or neonatal respiratory distress syndrome (NRDS), the results indicated that the presence of maternal diabetes was found to be effective in the development of hyaline membrane disease in infants, which was statistically significant. Matti et al.'s study showed that the incidence rate of respiratory distress syndrome (RDS) was significantly higher in infants with diabetic mothers than those with healthy mothers [17]. A study by Niesłuchowska identified maternal diabetes as one of the risk factors for the development of this disease in infants, and factors such as abnormal fetal circulation and fetal distress were also identified as other risk factors [18]. In a study by Li et al., the maternal diabetes included gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (PGDM) [19]. In a study by Kawakita et al., maternal diabetes led to an increase in respiratory complications in infants compared to non-diabetic patients [20].

In their study, Becquet et al. suggested that treatment of maternal diabetes with insulin during pregnancy would be an independent risk factor for neonatal respiratory distress [21]. The results of the present study showed that there was a statistically significant relationship between the maternal hypertension and hyaline membrane disease. In their study, Tubman et al. stated that high blood pressure in the mother had an effect on hyaline membrane disease [22]. The results of the present study indicated that the maternal addiction was effective in the development of hyaline membrane disease in infants, which was statistically significant.

According to the results obtained, the administration of corticosteroids led to a 0.378-fold decrease in HMD, which was statistically significant. In other words, corticosteroids have a protective role against HMD. These results are consistent with those of Liggines and Howie. They reported that maternal use of betamethasone would lead to a decrease in mortality as well as a decrease in the incidence rate of RDS [23].

The results of the present study are not consistent with the results of a study by Mehrpisheh et al. According to their research, they stated that infants whose mothers received corticosteroids during pregnancy needed more surfactants, which is inconsistent with our findings [24].

The results of the present study indicated that male gander increased the risk of hyaline membrane disease (HMD), which was statistically significant. In their study, Kim et al. reported that male gender was one of the risk factors for the increased development of HMD [25]. Also, a study by Wang et al. concluded that male gender is one of the factors affecting this disease [26]. In a study, Liu et al. found that male gender was one of the most important risk factors for neonates in increasing hyaline membrane development and would increase the relative risk of hyaline membrane disease 2.641 times more than girls [27]. It is believed that the female lung produces more surfactant than the male lung before delivery. The reasons for these findings may be as follows [28-31].

Androgens delay the secretion of lung fibroblasts by the fibroblast-pneumocyte factor (FPF), which can promote alveolar type II cells and delay the release of pulmonary surfactants.

Androgens slow down fetal lung growth by regulating epidermal growth factor signaling pathways and transforming growth factor beta. Estrogen enhances the pulmonary surfactant synthesis through the synthesis of phospholipids, lecithin, and surfactant proteins A and B. Estrogen also improves fetal lung growth by increasing the number of alveolar type II cells and by increasing the formation of lamellated bodies.

The results obtained from this study indicated that there was no statistically significant relationship between the type of delivery and the development of hyaline membrane disease in infants. In a study by Kim et al., cesarean section was identified as a risk factor, explaining that the fetus absorbs about one-third of the lung fluids during vaginal delivery, while appropriate absorption of fetal lung fluids in neonates who are delivered through cesarean section has not been achieved, and in addition, the spontaneous delivery process creates a system that results in the formation of surfactant that is eliminated during cesarean delivery [25]. In a study by Hansen et al., cesarean section was also identified as a risk factor for hyaline membrane disease [32]. Cesarean section was identified as one of the most important risk factors for hyaline membrane disease in a study by Liu et al. [27].

The sensitivity, specificity, negative predictive value, and positive predictive value of the GAST were reported to be100%, 40.7%, 100%, and 48.6%, respectively. Various studies have reported different sensitivity and specificity for negative test that would predict HMD itself. In a study in India by Chaudhari et al., a negative GAST (surfactant deficiency) in neonates with respiratory distress showed a sensitivity of 100%, a specificity of 70%, and a positive predictive value of 100% for the diagnosis of HMD. In this study, none of the patients had other respiratory diseases such as the transient tachypnea of the newborn (TTN) or pneumonia. They eventually concluded that this test can contribute to distinguishing HMD from other causes of respiratory distress in infants with high confidence [33].

In a study by Pena-Camarena et al., the sensitivity, specificity, negative predictive value, and positive predictive value of this test for HMD in neonates with respiratory distress were reported to be 97.5%, 77.1%, 98.2%, and 70.9%, respectively [34].

In another study on preterm infants with respiratory distress, the sensitivity, specificity, negative predictive value, and positive predictive value of this test for HMD were reported to be 40%, 63%, 88%, and 95%, respectively [35]. In a study by Amoa et al. on preterm infants with respiratory distress, the sensitivity, specificity, positive predictive value, and negative predictive value of this test for HMD were reported to be 40%, 95%, 63%, and 88%, respectively [36]. In the Babaei et al.'s study on preterm infants with respiratory distress, the sensitivity, specificity, positive predictive value, and negative predictive value of GAST for the diagnosis of HMD were 62.7%, 100%, 100%, and 80.5%, respectively. According to this finding, the GAST is an appropriate test to rule out the respiratory distress syndrome [37].

In a study by Golzar et al., the results obtained form GAST was found to be correlated with the diagnosis of HMD, and the sensitivity, specificity, positive predictive value, and negative predictive value of GAST for HMD diagnosis were reported to be 100%, 92%, 100%, and 92.3%, respectively. Based on this finding, the GAST is a reliable and simple test for the diagnosis of neonates with respiratory distress syndrome [38]. According to the study of Meemarian et al., the sensitivity, specificity, positive predictive value, and negative predictive value of GAST for HMD diagnosis were reported to be 60%, 75%, 15%, and 52%, respectively. Accordingly, GAST is not an appropriate method for the detection of surfactant deficiency and therefore, the study of respiratory distress syndrome should be based on clinical signs and radiological findings [24]. In the study of Mohammadi et al., the sensitivity, specificity, positive predictive value, and negative predictive value of GAST for HMD diagnosis were 100%, 66%, 64.5%, and 100%, respectively, and due to its high sensitivity and predictive value in ruling out HMD and lack of need for surfactant, the test are of great value [39].

In our study, the sensitivity, specificity, negative predictive value, and positive predictive value in the GAST were 100%, 40.7%, 100%, and 48.6%, respectively. By definition, sensitivity means the fraction of actual patients identified by the test as patient, and the specificity means the fraction of healthy individuals diagnosed by the test as healthy. Although a test whose sensitivity and specificity are 100% is an ideal test, there is often an inverse relationship between the two [40]. If we are to choose between the two, we should consider the purpose of the test. In cases where we are mostly looking for the disease and the false positive cases of the disease are less important, we use a high sensitivity test; and inversely, if the goal is only to find the real cases of the disease and it is not important to miss a few cases, a high specificity test is selected. When diagnosing hyaline membrane disease and determining the need for surfactant, we will seek more to find the real cases of the disease for early therapeutic intervention with the surfactant, and the higher specificity test is more valuable. Although all patients will need to be selected when using a high sensitivity and moderate specificity test for making a decision to administer surfactant, there is also the possibility of administering the surfactant to unnecessary patients. Therefore, it seems that the use of this test will reduce the unnecessary administration of surfactants [39]. The positive and negative predictive value of the test can also be helpful in interpreting a test. Positive predictive value means the probability that an individual with a positive test result will be truly patient and negative predictive value means the probability that an individual with negative test result will be truly healthy. In fact, high negative predictive value is helpful in ruling out the disease [39]. In our study, with respect to a negative predictive value of 100%, if the test showed surfactant adequacy, the diagnosis would be correct and the need for surfactant would be ruled out with the probability of 100%; and if the test showed surfactant deficiency, the infant would need surfactant with a probability of 48.6%. In this study, all infants weighing less than 1030 g as well as all infants younger than 29 weeks showed a negative test result and consequently received surfactant, and the presence or absence of a history of disease in their mothers had no effect on the surfactant reception. The most important limitations of this study were the low sample size of the study that may have an impact on the power of the study. It was also a descriptive study. Therefore, the specific limitations of these studies should be considered in analyzing the results.

Conclusion

The results of the present study showed that gastric aspirate shake test (GAST) can be used as a suitable tool in predicting the need for surfactant in preterm infants. Consideration is also needed for related factors. Considering the low sample size, further studies with larger sample sizes are recommended.

Abbreviations

GAST: gastric aspirate shake test.

NRDS: Neonatal respiratory distress syndrome

HMD: hyaline membrane disease

GDM: gestational diabetes mellitus

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