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Artículo original

Meconium aspiration syndrome, parental atopy and asthma symptoms in children under two years old

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RESUMEN

Objetivo: determinar la asociación entre síndrome de aspiración de meconio, atopia familiar y síntomas de asma en niños menores de dos años de edad.
Material y método: se incluyeron 136 expedientes de niños que habían sufrido síndrome de aspiración de meconio y se les dio seguimiento desde su nacimiento hasta los dos años de edad. El grupo control lo conformaron 136 niños sanos sin síndrome de aspiración de meconio.
Resultados: *grupo de niños con síndrome de aspiración de meconio:* el promedio de estancia hospitalaria en la unidad de cuidados intensivos neonatales fue de 5.91 ± 4.44 días y recibieron 65.5 ± 16.6 horas de oxígeno. La prevalencia de síntomas de asma durante el último año fue del 41.2%; 35.7% tuvieron antecedentes familiares de alergia (p = NS). La edad promedio al inicio de los síntomas de asma fue de 12.64 ± 6.96 meses; 78.6% de los niños incluidos en este grupo fue del sexo masculino (p=NS). *Grupo control:* 30.9% tuvieron episodios de pillido en los últimos 12 meses, 28.6% fueron del sexo masculino; 38.1% tuvieron antecedentes familiares de alergia (p=NS). La edad promedio al inicio de los síntomas de asma fue de 15.57 ± 6.05 meses.
Conclusiones: el síndrome de aspiración de meconio parece ser un factor de riesgo importante del inicio temprano de asma en niños menores de dos años de edad. Los datos muestran que la prevalencia de síntomas de asma fue mayor en el grupo de casos que en el grupo control. El riesgo de síntomas de asma se incrementa en niños con síndrome de aspiración de meconio o antecedentes familiares de alergia.
Palabras clave: síndrome de aspiración de meconio, asma, síntomas.

ABSTRACT

Objective: To determine the association among meconium aspiration syndrome, parental atopy and asthma symptoms in children younger than two years.
Material and methods: One hundred thirty six children who had suffered meconium aspiration syndrome were followed from birth to they were two years old. Control group included 136 healthy children without meconium aspiration syndrome.
Results: *Group of children with meconium aspiration syndrome:* The average hospital stay in neonatal intensive care unit was of 5.91 ± 4.44 days and were given 65.5 ± 16.6 hours of oxygen. Prevalence of asthma symptoms during the last year was of 41.2%; 35.7% had family history of allergies (p = NS). The average age at the beginning of asthma symptoms was of 12.64 ± 6.96 months; 78.6% of children were male. *Control group*: 30.9% had wheezing episodes during the last 12 months; 28.6% were male; 38.1% had family history of allergies (p = NS). The average age at the beginning of asthma symptoms was of 15.57 ± 6.05 months.
Conclusion: Aspiration of meconium seems to be an important risk factor of the early beginning of asthma symptoms in children younger than two years. Data shows that the prevalence of asthma symptoms was higher in case group than in control group. Asthma symptoms risk increases in children with aspiration meconium syndrome and family background of allergies.
Key words: meconium, aspiration, syndrome, asthma, symptoms.

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The function of airway epithelium is more than a simple anatomic barrier for protecting the airway smooth muscle.[1] Damage to airway epithelium during the early stages of life favors, in later years, the development of chronic respiratory diseases, such as asthma.[1-4] A major cause of damage to airway epithelium is the aspiration of meconium.[5,6] Meconium is a fluid constituted by gastrointestinal secretions, bile, biliary acid, mucus, pancreatic juice, cell debris, amniotic fluid and caseous vermix, lanugos, and swallowed blood.[7,8] The meconium aspiration syndrome is produced when the fluid is aspirated. This syndrome is a severe respiratory illness of full-term babies characterized by airway obstruction, gas trapping and ventilation imbalances, frequently requiring assisted mechanical ventilation, and the administration of oxygen. Twenty percent of newborns with meconium-stained amniotic fluid develop clinical diseases.[7-11] Some authors have found a high prevalence of asthma–related symptoms and airway hyper-reactivity in children older than six years with a history of severe respiratory distress caused by aspiration of meconium syndrome.[5,6,12] However, no studies have been conducted on the prevalence of asthma-related symptoms in children younger than two years that have had aspiration of meconium syndrome. This is relevant considering that an important percentage of cases of asthma starts before the age of two years and the causes for this phenomenon are still unclear.[13,14]

Several researchers have demonstrated that parental atopy is associated with an increased risk of asthma, suggesting that genetic factors play a central role in the development of asthma in childhood.[1,15,16,17]

The aim of this study was to assess the association between meconium aspiration syndrome, parental atopy and asthma symptoms in children younger than two years treated in a neonatal intensive care unit (NICU) due to severe respiratory distress caused by aspiration of meconium.

MATERIAL AND METHODS

We reviewed the files of children born during 2001, 2002 and 2003 admitted to the NICU at the Regional General Hospital, Mexican Institute of Social Security in Madero, Tamaulipas, Mexico in search of children diagnosed with aspiration of meconium syndrome. Neonates meeting the following inclusion criteria were included in the study: *1)* born and seen by specialists, gynecologists-obstetricians and pediatrics at the Tocosurgical Unit and admitted to the NICU at this hospital; *2)* gestational age over 38 weeks, *3)* diagnosed at birth with aspiration of meconium syndrome (having been found to be stained with amniotic fluid of thick green appearance and viscosity similar to pea soup) and corroborated with the presence of amniotic fluid in airways by aspiration visualized directly using a laryngoscope by a pediatrician, *4)* history of difficulty in breathing; *4)* oxygen therapy > 40%, and *5)* characteristic aspiration of meconium syndrome X-ray image. The study group was compared to a control group constituted by newborns without aspiration of meconium syndrome.

The parents of the newborns expected to participate in the study were provided a written and verbal explanation of the study objectives. Once consent was obtained, all participants were followed from birth with monthly visits for the first six months of extra-uterine life and afterwards, every three months, or if the children had respiratory disease.

Two questionnaires were used to register the information on participating children. One of the questionnaires was used to record data from birth such as: gestational age, birth type, gender, Apgar score, weight, height, days spent at the NICU and oxygen requirements.

The second questionnaire was designed to register mid- and long- term information. As a basis, an instrument used in the International Study of Asthma and Allergies in Childhood (ISAAC) was modified and validated through two pilot studies to adapt to our surroundings.[18] In each of the pilot studies, 20 persons were interviewed, 15 days apart, obtaining a 75% agreement. Through this instrument, information regarding age, weight, and height of the children was recorded. Parental atopy was defined as a history of maternal or paternal asthma, allergic rhinitis, or drug allergy. The presence of

smokers at home, whether the child was breastfed and its duration were also recorded, as well as any other disease suffered during visits.

In order to diminish any prejudice on behalf of the parents of the participating children (forgetfulness on data or confusing respiratory sounds), the presence of symptoms related to asthma were registered when parents responded positively to the question: In the last 12 months, has your child had wheezing sounds in his/her chest? asthma was diagnosed when parents answered affirmatively when asked: Has your physician told you your child suffers from asthma? We confirm asthma diagnosis and asthma symptoms by physical exploration, in asthma crisis.

Symptoms severity was classified as mild, moderate or severe based on *1)* the number of wheezing episodes suffered in the last 12 months; *2)* whether the symptoms interfered with sleeping, or *3)* if symptoms were so severe that the patient required adequate care at an emergency ward or hospital admission.

Statistical analysis

Simple frequencies and central tendency measures (means and standard deviations) were used to express the results. An analysis of the 2 x 2 contingency table (X^2 and OR) and 95% confidence intervals were used to estimate the risk of asthma for certain factors present in some children, comparing the meconium aspiration syndrome group to the control group.

RESULTS

During 2001, 2002 and 2003, 176 neonates were recorded as having meconium aspiration syndrome in the hospital medical records. Only 168 met the inclusion criteria for the study.

Thirty-two families of the 168 neonates with meconium aspiration syndrome moved from the address given at the time of the baby's birth and were lost. The cohort consisted of 136 newborns diagnosed with meconium aspiration syndrome, 51.5% were females and 48.5% males. The same gender proportion was seen in the control group.

An average hospital stay of 5.91 ± 4.44 days at the NICU was recorded receiving 65.5 ± 16.6 hours of oxygen. There were clear differences between meconium aspiration syndrome and control groups in relation to weight and body length at birth and gestational age (Table 1).

At follow up, the mean age for the children was of 22.35 ± 1.90 months (ranging between 19 to 24 months), in meconium aspiration syndrome and control groups. At this time, differences were found between the meconium aspiration syndrome and control groups with respect to height, weight and family history of allergies (Table 2).

Asthma-related symptoms were detected in 98 of the 272 children, 57.1% were male.

In meconium aspiration syndrome group 56 children had a history of wheezing in the last 12 months. 78.6% of these 56 children were males (p=NS), 35.7%

Table 1. Demographic characteristics of children who had suffered meconium aspiration syndrome and control group

	Meconium aspiration syndrome group		*Control group*	
Total	*n = 136*	*Range*	*n = 136*	*Range*
Gestation age (weeks ± SD)	40.30 ± 1.19	37-42	39.60 ± 1.40	38-42
Gender				
Male	66 (48.5%)		66 (48.5%)	
Female	70 (51.5%)		70 (51.5%)	
Apgar score				
At 1 min	3.60 ± 2.52	0-6	7.53 ± 0.96	5-9
At 5 min	7.05 ± 1.12	4-8	8.06 ± 0.35	7-9
At 10 min	8.56 ± 0.61	7-9	10 ± 0.0	10
Birth weight (g ± SD)	3,431.54 ± 653.83	1,575-4,975	3,198.03 ± 598.84	1,840-5,800
Birth height (cm ± SD)	51.94 ± 3.29	46-57	50.34 ± 2.39	43-57
Current height (cm ± SD)	86.56 ± 9.91	75-110	80.75 ± 5.35	63-94
Current weight (g ± SD)	12,505.88 ± 2,507.58	9,500-20,400	16,270 ± 1,269.47	1,500-8,900

SD: standard deviation.

Table 2. Clinical data at follow up of children with asthma symptoms who had suffered aspiration meconium syndrome and control group

Total	*Meconium aspiration syndrome group n = 56*	*Range*	*Control group n = 42*	*Range*
Gestation age (weeks ± SD)	40.50 ± 0.56	40-41	38.71 ± 1.20	38-41
Gender				
Male	44 (78.6%)		12 (28.56%)	
Female	12 (21.4%)		30 (71.40%)	
Apgar score	4.91 ± 1.46	2-6	8.00 ± 0.0	8-8
Current height (cm ± SD)	87.96 ± 9.35	78-107	83.29 ± 4.89	77-94
Current weight (g ± SD)	12,110.71 ± 1,041.10.58	10,800-14,000	11,442.86 ± 1,420.60	8,900-14,000
Family antecedent of allergy	20 (35.7%)		16 (38.7%)	
Personal antecedent of another allergic disease	56 (100%)		42 (100%)	
Presence of smokers at home	6 (10.7%)		0	
Age at start of asthma symptoms (months ± SD)	12.64 ± 6.89		15.57 ± 6.05	

SD: standard deviation.

had a family history of allergies (p = NS), 50% had been breastfed and 10.7% were exposed to second hand smoking at home (p = NS). The average age when symptoms related to asthma started was of 12.64 ± 6.89 months. A physician had diagnosed as asthmatic 28.6% of the children (Table 2).

In the control group, 42 had wheezing episodes in the last 12 months. Of these, 28.6% were males, 38.1% had a family history of allergies, and 85.7% had been breastfed. None was exposed to second hand smoking at home. The average age of the start of symptoms in this group of children was of 15.57 ± 6.05 months. However, a physician had previously diagnosed no one as having asthma.

In reference to the severity of the asthma symptoms, we found that all of the children, from both the meconium aspiration syndrome and control groups reported having one to three episodes of wheezing weekly, 14.3% of the children with meconium aspiration syndrome antecedent and asthma symptoms woke up at least one night a week due to asthma symptoms, none of these group required emergency care nor admission to a hospital due to asthma. On the other hand, 38.1% of the asthmatic children in the control group woke up at least one night a week, 14 had been treated in an emergency ward and 2 of them required admission due to asthma (Tables 3 and 4).

Table 3. Response distribution of questionnaire queries of the children with meconium aspiration syndrome antecedent and the control group

	Meconium aspiration syndrome group n (%)	*Control group n (%)*
Total population	136	136
Wheeze last 12 months	56 (41.2)	42 (30.9)
Sleep problems by wheeze	50 (36.8)	26 (19.1)
Woke up by wheeze	8 (5.9)	20 (14.7)
Asthma diagnosed by a physician	16 (11.8)	0
Waking with dry cough	36 (26.5)	34 (25)

Table 4. Clinical characteristics of the children with asthma symptoms of the meconium aspiration syndrome and control groups

	Meconium aspiration syndrome group n = 56 (%)	*Control group n = 42 (%)*	*p value*
Female sex	12 (21.4)	30 (71.4)	NS
Parental atopy	20 (35.7)	16 (38.1)	NS
Smokers at home	6 (10.7)	0	NS

DISCUSSION

Based on the sample of 136 children younger than two years, meconium aspiration syndrome seems

to be an important factor to the early beginning of asthma symptoms. Parental atopy is not associated to asthma symptoms in children younger than two years.

We found a 41.2% prevalence rate of asthma symptoms in children having had meconium aspiration syndrome. The results allow for a comparison with international reports from other authors such as Macfarlane and Heaf[6] who registered a prevalence of 39% in their study population of children older than six years and meconium aspiration syndrome survivors. Both results surpass the estimated overall prevalence in children of those groups of age (7.8-8.88 and 10-12%, respectively).[13,18,19] In order to determine the influence degree of the meconium aspiration syndrome over asthma symptoms, we assessed the effect of this disease when it is alone or combined with another risk factor such as parental atopy. Data show that meconium aspiration syndrome, alone or with other risk factors, does not mean a significant risk factor for the development of asthma symptoms in children younger than two years (p = NS). Nevertheless children of the meconium aspiration syndrome group started earlier asthma symptoms (12.64 ± 5.50 months) compared with children in control group (15.57 ± 7.57 months).

We are conscious that we only included children with severe meconium aspiration syndrome admitted to the NICU. Of these, we were able to locate only 80.95%. Therefore, this selection bias must be taken into account when interpreting the results since they cannot be generalized to all neonates with meconium aspiration syndrome admitted to the NICU. However, this situation should not subtract value to the results obtained since many of the cases are not due to the mentioned bias. This circumstance allows us to probably speculate that a large percentage of children with meconium aspiration syndrome, not included in our study, have also symptoms indicative of asthma.

It is widely known that asthma develops due to multiple factors.[15,20,21] Parental atopy is one of the factors strongly linked to the development of asthma.[16,17] Through several studies,[22,23] as those carried out by Tantisira, it has been shown that a family history of asthma represents a strong risk factor for the disease. In this study parental atopy is not associated to asthma symptoms. Thirty-six children with history of wheezing in the last 12 months had a direct relative with some kind of allergic disease (p = NS). Of these children 29.4% comprised the meconium aspiration syndrome group (p = NS) *versus* 39.7% of those in the control group (p = NS).

As previously mentioned, asthma results of a complex interaction of several factors.[16,23-28] It is important to keep in mind that although the prevalence of asthma symptoms in our population is greater that that reported for the general population of the same age, we also found a high prevalence of symptoms of asthma in children comprising the control group (30.9%) which only shows that in our environment there are a number of factors that favor the development of diseases such as asthma. As a final note, it is relevant to mention that the manifestations of asthma symptoms occurred early in children with meconium aspiration syndrome, in comparison to those in the control group, a situation that invites all to reflect further on the topic and pose additional hypotheses for clear clinical research.

Once again the phenomenon of an under-diagnosis is present. As Macfarlane[6] and other authors of larger community studies found,[18] we found a lack of adequate diagnosis of asthma in symptomatic children. Only 28.6% of 56 children with asthma symptoms were correctly diagnosed by a physician, but none from control group. This requires better training of physicians for the opportune diagnosis of asthma.

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