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MECONIUM-LIKE SUBSTANCE IN MIDTRIMESTER AMNIOTIC FLUID: SIGNIFICANCE FOR THE NEUROPSYCHOMOTOR EVOLUTION OF THE INFANT

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ABSTRACT

The state at birth and during the neonatal period, as well as the neuropsychomotor evolution, of 56 children with a normal karyotype, whose midtrimester amniotic fluid had meconium-like substance but a normal alpha-fetoprotein (AFP) level, were compared to those of two groups of infants with a normal karyotype and clear midtrimester amniotic fluid. One of these groups included 85 children born to mothers who had a history of uterine bleeding prior to amniocentesis, while the other was composed of 139 infants whose mothers had no history of bleeding. Among the mothers of the 56 children whose midtrimester amniotic fluid had meconium-like substance, 55% reported uterine bleeding prior to amniocentesis. Meconium-like substance in the midtrimester amniotic fluid has no prognostic value for abnormal neuropsychomotor evolution of the infant, provided that chromosomal aberrations are absent and the AFP level is normal.

INTRODUCTION

The amniotic fluid obtained at midtrimester amniocentesis for genetic evaluation of the fetus may sometimes exhibit a brown or green color. Excluding clear outlyers (Legge, 1981; Immken *et al.*, 1982; Alger *et al.*, 1984) the pooled data of 20,908 amniocenteses reported by several authors (Karp and Schiller, 1977; King *et al.*, 1978; Golbus *et al.*, 1979; Crandall *et al.*, 1980; Svigos *et al.*, 1981; Cruikshank *et al.*, 1983; Allen, 1985; Dacus *et al.*, 1985; Hess *et al.*, 1986) showed that 1.5% ± 0.08% of the amniotic fluids at the second trimester have such a pigmentation (Franchi-Pinto, 1993).

The brown or green color of the midtrimester amniotic fluid is usually attributed to meconium (Karp and Schiller, 1977; King *et al.*, 1978; Svigos *et al.*, 1981; Immken *et al.*, 1982; Abramovich and Gray, 1982; Allen, 1985). However, since some investigators have assumed that blood, either of fetal or maternal origin, may also be responsible for such pigmentation (Legge, 1981; Hankins *et al.*, 1984; Zorn *et al.*, 1986) we prefer to designate the brown or green substance seen in midtrimester amniotic fluid as meconium-like.

Uterine bleeding prior to amniocentesis is associated with the presence of meconium-like substance in midtrimester amniotic fluid. In fact, while this bleeding is found, on average, in 13% of the candidates for amniocentesis, the frequency of such a history may reach almost 70% among women whose midtrimester amniotic fluid is brown or green (Crandall *et al.*, 1980).

All cited authors agree that pregnancies with meconium-like substance in the midtrimester amniotic fluid will usually result in normal neonates, unless this fluid exhibits an elevated alpha-fetoprotein (AFP) concentration. The presence of a high AFP level in brown or green midtrimester amniotic fluid is an ominous sign, since it is always followed by spontaneous abortion (Golbus *et al.*, 1979; Cruikshank *et al.*, 1983).

The normal outcome of most cases with meconium-like substance in the midtrimester amniotic fluid has lead these authors to agree with Karp and Schiller (1977) that this finding may reflect only a transient episode of fetal distress without further consequences. Thus, in the absence of an elevated AFP level or an abnormal

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karyotype, a brown or green midtrimester amniotic fluid cannot be used to prognosticate either fetal death or the presence of congenital malformations in the newborn.

Nevertheless, no studies have been available concerning the neuropsychomotor evolution of infants whose midtrimester amniotic fluid exhibited meconium-like substance or whose mothers had uterine bleeding prior to amniocentesis, independently of the color of the amniotic fluid. Obviously, the optimal way to close this gap would be a clinical follow-up of these children, at least until the kindergarten years. Since this is, of course, a very difficult task we decided to circumvent the obstacles by carrying out a retrospective investigation.

SUBJECTS AND METHODS

The state at birth and during the neonatal period as well as the neuropsychomotor evolution of 280 children with a normal karyotype, whose mothers had been submitted to midtrimester amniocentesis for prenatal detection of chromosomal abnormalities from 1981 to 1989, were evaluated retrospectively on the basis of information given by these women. All mothers were Caucasoids, most of them (96%) living in southern or southeastern Brazilian states. All amniotic fluid samples were processed and visually assessed for pigmentation by one of us (W.P.Jr.) before and after being centrifuged.

The infants belonged to three groups:

Group A: Fifty six children whose midtrimester amniotic fluid had meconium-like substance and a normal AFP level, irrespective of the presence of blood cells. Fifty five percent of their mothers had a history of uterine bleeding prior to amniocentesis.

Group B: Eighty five children whose midtrimester amniotic fluid was clear, but who were born to mothers who had a history of uterine bleeding prior to amniocentesis.

Group C: One hundred and thirty nine children whose midtrimester amniotic fluid was clear, born to mothers with no history of uterine bleeding.

At it is seen, Groups B and C were controls of group A for investigating the effect of meconium-like substance in midtrimester amniotic fluid on neuropsychomotor evolution of the infants. On the other hand, group C was the control of group B for investigating whether uterine bleeding prior to amniocentesis could be associated with neuropsychomotor retardation. In all groups amniocentesis was most frequently performed before 18 weeks after the last menstrual period (78.6% in group A, 70.6% in group B and 74.1% in group C) in women aging on the average 34.8 ± 5.14 years at delivery (34.5 ± 5.69 years in group A, 34.6 ± 4.97 years in group B and 35.01 ± 5.14 ears in group C). Therefore, the three study groups may be considered as identical concerning both gestational age at amniocentesis ($\chi^2_{(2)} = 1.104$; $0.50 < P < 0.70$) and maternal age at delivery ($F_{(2;279)} = 0.22$; $P > 0.05$).

The following variables were compared:

1. Rupture of the amnion six or more hours prior to delivery.
2. Unusual fetal presentation: a) breach; b) shoulder.
3. Delivery with: a) forceps; b) cesarean section.
4. Cord around the neck.
5. Crying of the infant in the delivery room: a) late; b) absent.
6. Cyanosis at birth: a) extremities only; b) generalized.
7. Jaundice during the stay of the infant in the nursery.
8. Birth weight.
9. Inability to breast feed by the second day of life.
10. Long stay of the infant at the nursery: a) four to seven days; b) more than seven days.
11. Fever during stay in the nursery.
12. Seizures in the neonatal period.
13. Age at which the infant smiled.
14. Age at which the infant in a prone position was able to maintain the head erect and steady.
15. Age at which the infant was able to bring objects to the mouth for oral exploration.
16. Age at which the infant was able to assume a sitting position with help.
17. Age at which the infant was able to assume a sitting position without help.
18. Age at which the infant was able to creep.
19. Age at which the infant was able to walk.
20. Age of pronunciation of the first words.
21. Age of elaboration of complete phrases.
22. Age of sphincters control during the day.
23. Age of sphincters control at night.
24. Age of color identification.
25. Age of counting.

RESULTS AND DISCUSSION

Since the three groups of children did not show significant differences concerning variables 1 to 12 (Table I and II) it may be concluded that neither the presence of meconium-like substance in the amniotic fluid nor the uterine bleeding prior to amniocentesis influenced the state of the children either at birth or during the neonatal period.

For variables 13 to 25, which reflect the neuropsychomotor evolution of the infants, the results were not so homogeneous (Table II), as significant *F* tests were observed for variables 20, 21, 23 and 25. However, *t* tests showed that the average values of these variables for group A can be accepted as equal to those of group C (23

Table I - Frequencies of the qualitative variables analyzed in the three groups of children. (*)

Variable	Group A		Group B		Group C		Comparison
	No.	%	No.	%	No.	%	
1	43	37.2	67	37.3	104	32.7	$\chi^2_{(2)} = 0.493$; $0.70 < P < 0.80$
2	46	a) 4.3; b) 4.3	77	a) 7.8; b) 7.8	127	a) 9.4; b) 0.8	$\chi^2_{(4)} = 7.938$; $0.05 < P < 0.10$
3	54	a) 1.8; b) 66.7	83	a) 4.8; b) 71.1	136	a) 2.9; b) 72.8	$\chi^2_{(4)} = 2.064$; $0.70 < P < 0.80$
4	50	16.0	77	9.1	130	10.8	$\chi^2_{(2)} = 1.518$; $0.30 < P < 0.50$
5	53	a) 15.1; b) -	81	a) 11.1; b) 3.7	128	a) 9.4; b) 3.1	$\chi^2_{(4)} = 3.001$; $0.50 < P < 0.70$
6	45	a) 8.9; b) 15.5	66	a) 16.7; b) 15.1	115	a) 13.0; b) 11.3	$\chi^2_{(4)} = 2.269$; $0.50 < P < 0.70$
7	51	27.5	79	27.8	133	24.1	$\chi^2_{(2)} = 0.455$; $0.70 < P < 0.80$
9	51	5.9	81	7.4	137	5.1	$\chi^2_{(2)} = 0.651$; $0.70 < P < 0.80$
10	56	a) 13.5; b) 3.8	82	a) 24.4; b) 3.7	137	a) 16.8; b) 4.4	$\chi^2_{(4)} = 3.086$; $0.50 < P < 0.70$
11	50	2.0	74	2.3	137	2.2	$\chi^2_{(2)} = 0.081$; $0.90 < P < 0.98$
12	50	-	77	-	137	-	

(*) For definition of variables see Subjects and Methods.

Table II - Mean ($\bar{x}$) and standard deviation (s) of the quantitative variables analyzed in the three groups of children. (Variable no. 8 is expressed in grams. All others are expressed in months). (*)

Variables	Group A		Group B		Group C		F
	No.	$\bar{x} \pm s$	No.	$\bar{x} \pm s$	No.	$\bar{x} \pm s$	
8	52	3162 ± 626	80	3144 ± 609	136	3236 ± 554	0.72
13	40	1.82 ± 0.87	63	1.86 ± 0.88	97	2.03 ± 0.89	1.13
14	30	2.27 ± 0.91	57	2.39 ± 1.11	86	2.51 ± 1.20	0.58
15	26	3.54 ± 1.33	41	4.02 ± 1.15	64	4.03 ± 1.22	1.68
16	35	4.40 ± 1.40	55	4.73 ± 1.19	92	4.84 ± 1.31	2.90
17	33	6.15 ± 0.91	64	6.33 ± 1.14	98	6.30 ± 1.08	0.31
18	26	7.92 ± 2.10	63	8.25 ± 2.12	102	7.96 ± 1.56	0.57
19	37	11.86 ± 2.00	66	12.24 ± 2.52	112	12.30 ± 2.05	0.55
20	25	11.96 ± 3.22	54	15.33 ± 4.73	74	15.19 ± 4.58	5.73***
21	18	18.22 ± 4.72	39	22.13 ± 5.61	70	21.23 ± 5.28	3.39*
22	20	23.35 ± 6.00	38	24.08 ± 4.03	92	22.59 ± 5.29	1.18
23	17	27.00 ± 10.30	32	31.22 ± 8.36	71	26.54 ± 6.54	4.25**
24	19	29.63 ± 6.81	31	31.42 ± 11.50	66	28.39 ± 6.78	1.44
25	19	34.68 ± 12.08	30	38.20 ± 14.35	40	28.62 ± 8.16	6.26****

*P < 0.05; **P < 0.025; ***P < 0.01; ****P < 0.005.

(*) For definition of variables see Subjects and Methods.

and 25) or even lower than those presented by the other two groups (20 and 21). Therefore, it may be concluded that the meconium-like substance in the midtrimester amniotic fluid has no prognostic value for abnormal neuropsychomotor evolution of the infant, provided that chromosomal aberrations are absent and the AFP level is normal.

In contrast, the significant F tests found for variables 23 and 25 were due to higher average values presented by group B, which are children whose

midtrimester amniotic fluid was clear, but who were born to mothers with uterine bleeding prior to amniocentesis.

Although there was a small excess of significant values beyond those expected by chance alone, this should not be taken as very important without further investigation, due to the fact that these variables are of a somewhat subjective nature, and that 55% of group A mothers also had uterine bleeding prior to amniocentesis.

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RESUMO

As condições ao nascimento e no período neonatal bem como a evolução neuropsicomotora de 56 crianças com cariótipo normal, cujo fluido amniótico no segundo trimestre de gestação tinha substância meconial-símile mas nível de AFP normal, foram comparadas com aquelas de dois grupos de crianças com cariótipo normal cujo fluído amniótico havia sido claro. Um desses grupos incluiu 85 crianças geradas por mães com história de sangramento uterino antes da amniocentese, enquanto o outro foi composto por 139 crianças cujas mães não tinham tal história. Dentre as mães das 56 crianças cujo fluído amniótico apresentara substância meconial-símile, 55% tiveram sangramento uterino antes da amniocentese. A substância meconial-símile no fluído amniótico do segundo trimestre de gestação não tem valor para prognosticar evolução neuropsicomotora anormal, desde que não se detectem aberrações cromossômicas e o nível de AFP seja normal.

REFERENCES

Abramovich, D.R. and **Gray, E.S.** (1982). Physiologic fetal defecation in midpregnancy. *Obstet. Gynecol. 60*: 294-296.

Alger, L.S., Kisner, H.J. and **Nagey, D.A.** (1984). The presence of a meconium-like substance in second-trimester amniotic fluid. *Am. J. Obstet. Gynecol. 150*: 380-385.

Allen, R. (1985). The significance of meconium in midtrimester genetic amniocentesis. *Am. J. Obstet. Gynecol. 152*: 413-417.

Crandall, B.F., Howard, J., Lebherz, T.B., Rubinstein, L., Sample, W.F. and **Sarti, D.** (1980). Follow-up of 2000 second-trimester amniocentesis. *Obstet. Gynecol. 56*: 625-628.

Cruikshank, D.P., Varner, M.W., Cruikshank, J.E., Grant, S.S. and **Donnelly, E.** (1983). Midtrimester amniocentesis: An analysis of 923 cases with neonatal follow-up. *Am. J. Obstet. Gynecol. 146*: 204-211.

Dacus, J.V., Wilroy, R.S., Summitt, R.L., Garbaciak, J.A., Abdella, T.N., Spinnato, J.A., Luthardt, J.A., Flinn, G.S. and **Lewis, B.A.** (1985). Genetic amniocentesis: a twelve years experience. *Am. J. Med. Gen. 20*: 443-452.

Franchi-Pinto, C. (1993). *Significado do fluido amniótico meconial no segundo trimestre da gestação.* Master's Thesis, UNICAMP, Campinas.

Golbus, M.S., Loughamn, W.D., Epstein, C.J., Halbasch, G., Stephens, J.D. and **Hall, B.C.** (1979). Prenatal genetic diagnosis in 3000 amniocentesis. *N. Engl. J. Med. 300*: 157-163.

Hankins, G.C.B., Rowe, J., Quirk Jr., J.G., Trubey, R. and **Strickland, D.M.** (1984). Significance of brown and/or green amniotic fluid at the time of second trimester genetic amniocentesis. *Obstet. Gynecol. 64*: 353-358.

Hess, L.W., Anderson, R.L. and **Golbus, M.S.** (1986). Significance of opaque discolored amniotic fluid at second trimester amniocentesis. *Obstet. Gynecol. 67*: 44-46.

Immken, L., Lee, M., Stewart, R. and **Kabach, M.M.** (1982). Significance of meconium stained fluid in midtrimester amniocentesis. *Birth Defects: Original Article Series 18*: 187-190.

Karp, L.E. and **Schiller, H.S.** (1977). Meconium staining of amniotic fluid at midtrimester amniocentesis. *Obstet. Gynecol. 50* (Suppl.): 47-49.

King, C.R., Prescott, G. and **Pernoll, M.** (1978). Significance of meconium in midtrimester diagnostic amniocentesis. *Am. J. Obstet. Gynecol. 132*: 667-669.

Legge, M. (1981). Dark brown amniotic fluid-identification of contributing pigments. *Br. J. Obstet. Gynaecol. 88*: 632-634.

Svigos, J.M., Stewart-Rattray, S.G. and **Pridmore, B.R.** (1981). Meconium-stained liquor at second-trimester amniocentesis - Is it significant? *Aust. N.Z.J. Obstet. Gynaecol. 21*: 5-6.

Zorn, E.M., Hanson, F.W., Greve, C., Phelps-Sandall, B. and **Tennont, F.R.** (1986). Analysis of the significance of discolored amniotic fluid detected at midtrimester amniocentesis. *Am. J. Obstet. Gynecol. 154*: 1234-1240.

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