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Investigation of the relationship between low Apgar scores and early neonatal thyroid function

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Abstract

Background: The aim of the present study was to assess the effects of low Apgar scores on perinatal thyroid function.

Methods: Forty full-term infants delivered by the normal spontaneous vaginal route were enrolled into the study. All babies had 1 and 5 min Apgar scores below 4. The control group consisted of 26 full-term healthy neonates. Cord blood and serum tri-iodothyronine (T_3), thyroxine (T_4), reverse tri-iodothyronine (rT_3), free thyroxine (FT_4), thyroid-stimulating hormone (TSH) and thyroid-binding globulin (TBG) determinations were performed by an enzyme immunoassay method.

Results: The mean values of FT_4 and T_4 observed in the cord blood of the study group were significantly lower compared with matched controls, whereas the mean TSH values were significantly higher. There were no differences in concentrations of T_3, rT_3 and TBG between the two groups.

Conclusions: These results demonstrate the existence of transient hypothyroidism at birth in babies with Apgar scores below 4 delivered by the spontaneous vaginal route.

Key words Apgar, hypothyroidism, perinatology.

The Apgar score is a widely used method for the rapid assessment and immediate early postnatal follow-up of the neonate. Prematurity, maternal drug intake, infections, neuromuscular and cerebral malformations and hypoxia may cause a low Apgar score.

Due to birth stress, there is a gradual rise in thyroid-stimulating hormone (TSH) levels after birth, reaching a peak at 30 min. After 3 days of life, TSH levels begin to decline due to normal feed-back mechanisms. The rise in TSH affects thyroxine (T_4) levels, therefore causing a dramatic increase in tri-iodothyronine (T_3) levels in the first few hours of life, which return to normal levels after 1 week.[1]

In the early period of perinatal hypoxia, autoregulatory mechanisms provide a decrease in blood flow to organs except for the heart and brain.[1] During perinatal hypoxia, functional abnormalities of the neonatal thyroid have been described previously.[2] However the relationship between low Apgar scores and thyroid function has not been assessed in detail. We tried to assess how thyroid function is affected in neonates with low Apgar scores and to determine whether low Apgar scores could be accepted as a possible predictor of perinatal hypoxia.

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Methods

The present study was conducted at the Department of Pediatrics of Zeynep Kamil Hospital between March and June 1998 . During this period, 40 term neonates (28 males and 12 females) who were delivered by the normal spontaneous vaginal route and who had Apgar scores below 4 at 1 and 5 min constituted the study group. The control group comprised 26 healthy neonates (15 females, 11 males) who were also delivered by the normal spontaneous vaginal route in the same delivery room. Their Apgar scores were at least 6–8 and 8–10 at 1 and 5 min, respectively. Gestational ages of all neonates were determined by maternal history and the Ballard scoring system.

White blood cell count, C-reactive protein levels and cultures, if needed, were obtained at entry to the study for all neonates. Cases with any signs of infection or congenital malformation and those with mothers with a history of thyroid disease, alcohol consumption, smoking or drug abuse were not included in the study.

Table 1 Comparison of tri-iodothyronine, thyroxine, rT_3, FT_4, thyroid-stimulating hormone and TBG in the study and control groups

	T_3 (ng/mL)	T_4 (μg/dL)	rT_3 (nmol/L)	FT_4 (ng/dL)	TSH (μU/mL)	TBG (mg/L)
Control group ($n = 28$)						
1 day	0.84 ± 0.15	9.1 ± 1.4	2.4 ± 0.4	1.0 ± 0.3	8.11 ± 3.42	50.5 ± 14.5
5 days	1.8 ± 0.3	11.52 ± 2.78	1.7 ± 0.2	1.17 ± 0.36	20.61 ± 14.42	46.6 ± 10.6
Study group ($n = 40$)						
1 day	0.81 ± 0.17	8.04 ± 1.37*	2.2 ± 0.3	0.78 ± 0.10**	13.03 ± 9.77*	49.5 ± 12.9
5 days	1.55 ± 0.38*	9.69 ± 2.80*	1.9 ± 0.5	1.03 ± 0.32	23.56 ± 13.42	48.8 ± 11.8

Results are the mean ± 1SD. *$P < 0.01$, **$P < 0.001$ compared with healthy infants.

T_3, tri-iodothyronine; T_4, thyroxine; rT_3, reverse tri-iodothyronine; FT_4, free thyroxine; TSH, thyroid-stimulating hormone; TBG, thyroid-binding globulin.

All neonates were discharged from hospital 48 h after birth, provided that they had normal findings on physical examination and a control examination was arranged at the 5th day of life. Cord blood samples were collected at birth and venous blood samples were obtained at the control visit. After centrifugation, serum was pipetted and stored at –20°C until hormone level determinations were performed.

Cord blood and serum T_3, T_4, rT_3, FT_4, TSH and TBG determinations were performed by an enzyme immunoassay method with commercially available kits (Boehringer Mannheim, Mannheim, Germany). The measurement of T_3, T_4, rT_3 and FT_4 levels was performed using an ELISA method, which works on the principle of competition with streptavidine technology. The measurement of TSH and TBG levels was performed with ELISA/one-step sandwich method using streptavidine technology.

The study was approved by the local ethics committee and written informed consent was obtained from the parents of all children before entry into the study.

Statistical analysis was performed using the SPSS statistical package program (SPSS Inc., Chicago, IL, USA) for personal computers.

Results

Mean birth weight (range) in the study and control groups was 3.1 ± 0.3 (2.6–4.0 kg) and 3.3 ± 0.3 kg (2.6–4.2 kg), respectively.

The plasma concentrations of thyroid parameters, such as TSH, TBG, T_3, T_4, rT_3 and FT_4, are shown in Table 1.

When compared with the control group, cord blood TSH levels in the study group were significantly higher ($P < 0.01$) and cord blood T_4 ($P < 0.01$) and FT_4 ($P < 0.001$) levels were significantly lower. There was no difference between the two groups with respect to T_3, rT_3 and TBG levels.

Discussion

Thyroid hormone production (especially iodine transport through the cell membrane) is an energy requiring and rate-limiting step in biosynthesis. The thyroid gland has an abundant blood supply with 5 mL blood/g tissue per min.[1] The effect of low Apgar scores on perinatal thyroid function has not been investigated in detail. Low Apgar scores in the first minute do not necessarily correlate with a poor prognosis for the infant, but 5 min Apgar scores and, in particular, the difference between the 1 and 5 min Apgar scores is a strong predictor of the effectiveness of resuscitation.[3] In the present study, we investigated the effect of Apgar scores below 4 on thyroid function.

Several previously published studies have attempted to evaluate the influence of perinatal factors on neonatal thyroid function. Wilson *et al*. have shown that FT_4 was significantly lower in neonates with a low Apgar score.[4] Tahirovic reported transient hypothyroxinemia in the cord blood of asphyxiated infants born by emergency Cesarean section.[5]

In contrast, Franklin *et al*.[6] and Erenberg[2] did not find a significant effect of asphyxia at birth on neonatal thyroid function.

In accordance with the studies of Tahirovic and Wilson *et al.*,[4,5] cord blood T_4 and FT_4 levels of infants with Apgar scores below 4 in the present study were low when compared with the control group. However, in contrast with normal TSH levels in the study of Tahirovic, the cord blood TSH levels of the study group in the present study were significantly higher than in the control group. Tahirovic speculated that his findings were due to a decrease in hypothalamic thyrotropin-releasing hormone (TRH) secretion related to both hypoxia and stress.[5,7,8] We think that Apgar scores below 4 may cause cellular damage in the thyroid, which, in turn, stimulates the pituitary gland by corrupting thyroid hormone synthesis. Therefore, we attributed normal

thyroid function at the 5th day to functional increases of hormone production in the thyroid gland. The results of the present study are consistent with those of previous studies in patients with severe non-thyroidal illnesses, which have demonstrated low FT_4 and T_4.[4]

When compared with the control group, the 5th day T_3 levels of the study group were found to be significantly lower. Low Apgar scores must have influenced the peripheral metabolism of thyroid hormones.

In conclusion, the results of the present study demonstrate the presence of transient hypothyroidism at birth in babies with Apgar scores below 4 delivered by normal spontaneous labor. In our opinion, the practical significance of these findings is that Apgar scores below 4 affect the thyroid gland, possibly because of effects on the hypothalamo–pituitary axis, but thyroid functions return to normal in a relatively short time due to the intact pituitary gland. However, in cases where low Apgar scores are associated with central nervous system damage, the pituitary gland may not be able to react properly. Hence, we suggest a complete investigation of thyroid function in all patients exposed to significant hypoxia and/or low Apgar scores with neurological findings.

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