Characteristics and Outcome of Neonates with Congenital Hypothyroidism Born after In Vitro Fertilisation (IVF)

Giorgi V1, Kanaka-Gantenbein C1,2, Ardati JD1, Platis D1, Choularias G2, Kourkouti C2, Kosteria I1, Gika A1, Illiadi A1,2, Chrousos GP2, Girginoudis P1, Voutetakis A1,2

1 Department of Biochemistry, Institute of Child Health, Athens, Greece
2 Division of Endocrinology, Metabolism and Diabetes, 1st Department of Pediatrics, “Aghia Sophia” Children’s Hospital, Athens University School of Medicine

Background knowledge

In vitro fertilisation (IVF) has been widely used during the last decades. Increased susceptibility to birth defects and a higher cardiometabolic risk in children born after IVF than naturally conceived (NC) children have been reported. Also, a higher incidence of hypothyrotoxicemia has been noted in children born after IVF with respect to NC children and has been attributed to an epigenetic modification of the TSH set-point.

The National Greek Neonatal CH screening program was initiated in 1980 and is carried out by a single laboratory that receives and tests the Guthrie cards from all maternity hospitals. The program initially covered the Athens Metropolitan area but quickly expanded and covered the entire country. Over the last 35 years, more than 3,690,000 neonates have been screened using a variety of TSH screening methods.

Objective and hypothesis

To retrospectively evaluate the main characteristics and outcome of children born after IVF and diagnosed with CH.

Patients and Methods

Data from the medical records of children diagnosed with CH by the Greek Neonatal CH screening program were reviewed.

Results and Discussion

A total of 1474 children with CH were analyzed. Of these, 200 neonates (13.5%) were born following IVF (117 boys and 83 girls; ratio 1:1.4). 80% of neonates born after IVF were multinots, 85% were premature (<37 gestational week) and 82% had a birth weight below 2500 gr (Table 1 and Figure1).

TSH values at diagnosis: 15% had a TSH > 20 mU/L, 26% between 10 and 20 mU/L and 50% below 10 mU/L (mean 36.1 115 mU/L). The probability of CH to be transient is inversely related to the initial TSH values in females whereas in males seems independent (Figure 2).

Gestational age: 57% of neonates were moderate to late preterm and 28% were very to extreme preterm. The probability of CH to be transient is inversely related to the weeks of gestation in females whereas in males the percent is more consistent between subgroups (Figure 3).

Thyroid ultrasonography: imaging data were available to analyze in 156 patients. Diagnoses were categorized as normal, ambiguous or as anatomical defect (absence, ectopy etc). A diagnosis of “ambiguous” was used in the case of very small thyroid glands, low normal size of thyroid with respect to age, prominent heterogeneity etc. In only 5% of CH patients born after IVF ultrasonography revealed an anatomical defect of the thyroid gland (Figure 4).

Pertinent long-term data were available in 141 patients (81 boys and 60 girls). Their age at the time of the analysis was 7.53 ± 3.1 yrs (>1 year: 140 > 3 yrs: 133)

With respect to the outcome, the overall percent of permanent CH was 56%, 51% in males and 83% in females and of transient CH was 44%, 49% in males and only 37% in females (Table 1).

Conclusions

Children born after IVF constitute a relatively large subgroup (13.5%) of children with CH, with a notable male predominance (1:4.1). Most of the children where born prematurely (85%) with a low birth weight (82%) following high risk pregnancies (multinots 80%). Anatomical thyroid defects are rare (present in only 5% of patients). Although hypothyroidism at diagnosis is mild based on TSH values, in 50% of males and 63% of females born after IVF, a certain degree of dysfunction of the Hypothalamic-Pituitary-Thyroid-axis seems to persist. The reason of the gender dimorphism with respect to the diagnosis and outcome is not apparent.