Does Ventriculoperitoneal Shunting Improve Thyroid Hormone Levels in Hydrocephalic Newborns?

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Key Words

Hydrocephalus · Hypothyroidism · Thyroid hormones ·
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Abstract

Objective/Aim: The aim of this report was to investigate the effect of ventriculoperitoneal shunt insertion for the treatment of hydrocephalus on thyroid hormones in the first 3 months of life. **Methods:** Thyroid-stimulating hormone (TSH), free T3 (fT3), and free T4 (fT4) levels were compared at 7 days (preoperatively) and at 30 and 90 days (postoperatively) after birth between 25 ventriculoperitoneal shunt-inserted hydrocephalic newborns and 20 healthy newborns. **Results:** The TSH level at 7 days was higher in the hydrocephalic patient group (6.33 μ U) compared to the control group (3.76 μ U). This value was significantly decreased at 90 days in the ventriculoperitoneal shunt-inserted newborns (2.35 μ U) compared to the control group (3.33 μ U; $p < 0.05$). There were no significant differences between time points for fT4 and fT3 values in the patient group or for TSH, fT4, and fT3 values in the control group. **Conclusion:** We propose that a ventriculoperitoneal shunt inserted in the early period of life may have beneficial effects on thyroid hormones.

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Introduction

While the incidence of isolated hydrocephalus is 1–1.5 per 1,000 live births, its incidence associated with other congenital or acquired neurological pathologies is 3–4 per 1,000 live births [1, 2]. Ventricular dilatation caused by hydrocephalus has harmful effects on the developing brain in newborns. Major effects of hydrocephalus include: cortical thinning, white matter atrophy, decreased cerebral perfusion, brain edema, compression of small blood vessels in the periventricular white matter, destruction of axons, and loss of the connective tissue between neurons [3, 4].

The effect of increased intracranial pressure (ICP) due to hydrocephalus on thyroid functions is not clear. However, previous studies have emphasized that patients with hydrocephalus might have endocrinological abnormalities [5–8], although these studies did not evaluate the endocrinological effects of the ventriculoperitoneal (VP) shunt in the first 3 months of life.

Diffuse damage of the cellular, anatomical, and biochemical structure of the brain created by hydrocephalus also affects hypothalamic and pituitary functions [3]. However, how the presence of a VP shunt affects the hypothalamic-pituitary-thyroid axis in the first 3 months of

Fig. 1. Mean TSH values of the patient and control groups at 3 different time points. In infants with hydrocephalus, TSH levels were significantly (* $p < 0.05$) decreased at both 30 and 90 days compared to the values at 7 days.

life has not been studied extensively. For that reason, the aim of this study was to evaluate the effect of VP shunting on thyroid hormones in hydrocephalic newborns.

Materials and Methods

Study Design and Subject Selection

Twenty-five isolated congenital hydrocephalic newborns were followed up as the patient group, and 20 healthy newborns were the control group. Forty-five newborns were followed, based on laboratory and clinical indicators, by the Department of Pediatric Endocrinology. Neither the 25 hydrocephalic patients nor the 20 healthy newborns required endocrinological treatment. The 25 isolated congenital hydrocephalic newborns underwent insertion of a VP shunt within the first 10 days of life. These newborns were screened and followed up for congenital hypothyroidism (CH). Informed consent was obtained from the legal guardians, and permission from the local ethics committee was granted for this study to proceed.

In this study, the levels of thyroid-stimulating hormone (TSH), free T4 (fT4), and free T3 (fT3) in newborns in both the patient group and the control group were evaluated as indicators of thyroid function at 7, 30, and 90 days after birth. In the hydrocephalic patients, the level at 7 days was evaluated before the shunt operation.

The newborns in both groups did not receive any medications, such as corticosteroids, aspirin, phenytoin, β -blockers, or dopamine, which might have influenced thyroid hormone levels. Also, iodinated contrast agents were not given before blood samples were taken, and no other cause of hypothyroidism was found in either group. Infants with TORCH infection, other congenital anomalies, or syndromic diseases, and infants whose mothers had used drugs which might have influenced thyroid function, were excluded from this study.

Table 1. Thyroid hormone levels and statistical analysis based on the t test

	RoNV	Patient group (n = 25)	Control group (n = 20)	p
TSH, μ IU/ml				
7 days	<5.5	6.33 $\pm$ 6.06	3.76 $\pm$ 2.23	0.041
30 days	2–4.7	2.91 $\pm$ 2.82	3.59 $\pm$ 1.76	0.376
90 days	1.7–2	2.35 $\pm$ 1.28	3.33 $\pm$ 1.89	0.035
fT4, ng/dl				
7 days	1.1–2.6	1.22 $\pm$ 0.33	1.17 $\pm$ 0.63	0.742
30 days	1.2–1.9	1.99 $\pm$ 2.76	1.02 $\pm$ 0.28	0.150
90 days	0.9–2.3	1.12 $\pm$ 0.26	1.28 $\pm$ 0.35	0.108
fT3, pg/ml				
7 days	2–5.6	4.52 $\pm$ 2.13	2.96 $\pm$ 1.56	0.012
30 days	3.1–4.9	5.09 $\pm$ 1.39	3.06 $\pm$ 1.4	0.000
90 days	1.6–5.2	4.16 $\pm$ 1.05	3.51 $\pm$ 1.50	0.102

Values are presented as means $\pm$ SD unless otherwise stated. RoNV = Range of normal values [20].

Methods

In addition to neurological examinations, hydrocephalus was diagnosed via magnetic resonance imaging and/or computed brain tomography, as well as by evaluation of the head circumference. Samples of venous blood (1 ml) were collected from infants for evaluation of thyroid hormone tests. Thyroid tests were performed based on the chemiluminescence method using a Siemens IMMULITE 2000 system (Flanders, N.J., USA) in our hospital's central laboratory. TSH, fT4, and fT3 levels in serum were recorded (expressed in μ IU, ng/dl, and pg/ml, respectively).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) for Windows (version 17.0) was used for statistical analysis. Parametric data were analyzed using a t test, and percentage data were analyzed using a χ^2 test; correlation and analysis of variance to show the relationship between results were used. Results are expressed as means and 95% CI, and $p < 0.05$ was considered statistically significant.

Results

The levels of TSH and fT4 were normal at 3 months of follow-up in both the patient group and the control group. The mean TSH level at 7 days in the patient and control groups was 6.33 and 3.76 μ IU, respectively. Based on the t tests of the patient and control groups (7, 30, and 90 days after birth), the mean levels of TSH and fT3 at 7 days, and of fT3 at 30 days, were higher in the patient group than in the control group (table 1). However, the levels of TSH at 90 days were lower in the patient group

(2.35 μ IU) compared to the control group (3.33 μ IU; $p < 0.05$; table 1).

The TSH values of the patient and control groups at the 3 different time points are shown in figure 1. In infants with hydrocephalus, TSH levels were significantly decreased both at 30 and at 90 days compared to the values at 7 days ($p < 0.05$). However, there were no significant differences between time points for fT4 and fT3 values in the patient group, or for TSH, fT4, and fT3 values in the control group.

Discussion

The thyroid hormone is an essential hormone for mammalian development. In cases of thyroid hormone deficiency, the abnormality (known as cretinism) affects the development of all organ systems [9]. The brain is particularly affected and motor deficits, ataxia, spasticity, deafness, and mental retardation due to brain damage may develop. In addition, while treatment started immediately after birth can ensure normal development, treatment started after this important period is not so effective for children with cretinism [10]. Thyroid hormone screening in hydrocephalic children may be overlooked. Moreover, if treatment of CH fails in the early period in hydrocephalic patients, the effects on brain damage with hydrocephalus may be additive. VP shunt surgery and sufficient provision to ensure a normal thyroid hormone profile in an early period in these children will help to protect the hydrocephalic brain.

Many hormonal disturbances associated with increased ICP have been investigated in head trauma, but there is no clear consensus on this issue [11, 12]. Despite this, endocrinological evaluation of patients with head trauma is important for assessment of their progression. Hormone profiles in coma patients due to head trauma were investigated, and decreases in levels of TSH, luteinizing hormone, and follicle-stimulating hormone were shown, with no change in levels of growth hormone or prolactin [11, 12]. Matsuura et al. [10] reported increased prolactin levels and no change in TSH levels in patients with acute head trauma. Disruption of the hypothalamic-pituitary axis after a traumatic head injury may occur due to direct injury or as a result of neuroendocrinological effects of catecholamines and cytokines or systemic inflammation [13, 14]. Another study regarding pituitary function in patients with normal pressure hydrocephalus before and after neurosurgical correction showed that normal pressure hydrocephalus causes pituitary dysfunction

because of intermittent bursts of intracranial hypertension [15]. Hormone secretions are episodic and blood samples were obtained at different times, and the results may also be explained by specific mechanisms that lead to the disruption of the hypothalamic-pituitary axis. We propose that hormonal disturbances in hydrocephalus may be due to injury of either isolated or combined pituitary hormone-secreting cells.

It has been shown that neuropeptides may also play an important role in adults with dementia. Neuropeptide Y, somatostatin, and corticotropin-releasing factor are neuropeptides involved in cognitive functions. It was reported that concentrations of neuropeptide Y and somatostatin were decreased in patients with normal pressure hydrocephalus, and that levels of these neuropeptides after shunt surgery were normal [16]. Improvements in cognitive function observed after shunt insertion were considered to be associated with normalization of the levels of these neuropeptides [16]. Because assessment of cognitive functions in newborns was not possible, these studies in adults may provide insight regarding the pathological effect of hydrocephalus at cellular, anatomical, and biochemical levels.

Some papers have revealed endocrinological improvements in patients after VP shunt surgery [17, 18]. Similarly, increased gonadotropin levels and a regular menstrual cycle have been reported in patients with increased ICP and pituitary hormone disturbances associated with convexity meningioma after tumor surgery [19].

Diffuse biochemical and anatomical changes occurring in hydrocephalus may affect the hypothalamic-pituitary axis, followed by effects on the function of the thyroid gland. In this study, postoperative TSH values in hydrocephalic newborns recovered more quickly after VP shunt surgery compared to preoperative values and the control group. These cases indicate that hydrocephalus may adversely affect TSH levels, and that insertion of a VP shunt facilitates a more physiological situation for the thyroid gland. Thus, hydrocephalic newborns should undergo a full endocrinological assessment. While insertion of a VP shunt decreases brain edema, ICP, and inflammation and increases the cerebral blood flow and myelination in the early period, it may also facilitate a better physiological environment for the hypothalamic-pituitary axis, with benefits for the circadian rhythm and improvements in cognitive function in the late period.

There has been significant development over the last century in the treatment of hydrocephalus, and early diagnosis, treatment, and follow-up of these patients is now more successful. We recommend that CH, which causes

irreversible brain parenchymal injury and mental retardation in hydrocephalic newborns, should not be ignored, and we propose that a VP shunt inserted in an early period may have a beneficial effect on thyroid hormones.

Disclosure Statement

The authors have nothing to disclose.

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