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A prospective observational study to evaluate the pattern of pituitary dysfunction in patients with acute phase of subarachnoid haemorrhage

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Abstract

Introduction: SAH has been predicted as a risk for hypothalamic–pituitary dysfunction. Pattern of hormonal impairments has been shown to differ substantially. Cause of these functional problems remains, at least in part, unclear and many of these symptoms are similar to those occurring in patients with untreated hypopituitarism.

Aim and objectives: The present study was performed to observe the pattern of pituitary dysfunction in patients with acute phase of subarachnoid haemorrhage, who were admitted in the intensive care unit of a tertiary care hospital.

Materials and Methods: Anterior pituitary hormones were analysed in 98 patients within 72 h after spontaneous SAH. Out of 98 patients in our study, 29 **(29.5%)** patients had no hormonal dysfunction, 21 (22%) patients had single hormonal dysfunction, 26 (26%) patients had abnormality of two hormones and 21 (22%) patients had more than two hormonal dysfunction. found subclinical hypothyroid in 9 patients with mean TSH levels of 6.16±1.41 µIU/ml. In 4 patients TSH levels were >10 µIU/ml. 24 male patients were having low testosterone levels. Low estradiol was detected in 9 (30.8%) female patients.

Conclusion: Our study confirmed that anterior pituitary hormonal deficiency occur in a substantial number of patients at initial stage of sub arachnoid haemorrhage, whether this occurs later on needs to be followed and studied. Thus it is important to evaluate these patients continuously with periodic endocrine examination and follow up.

Keywords: SAH, Aneurysmal subarachnoid haemorrhage; endocrine dysfunction; Hypothallamo-pituitary axis, Neuro-critical care

Introduction

Aneurysmal subarachnoid haemorrhage (SAH) has been predicted as a risk for hypothalamic–pituitary dysfunction, given the proximity of these structures to the arterial circle of Willis.[1] SAH may be due to post haemorrhagic local tissue pressure changes, toxic effects of the extravagated

blood, ischemia caused by vasospasm, high intracranial pressure, hydrocephalus, or local destruction during cerebral surgery. This in turn leads to the compression of the hypothalamic–pituitary axis and endocrine disturbances. This happens in particular for aneurysms of the anterior communicating artery, the most common site of aneurysms, because arteries derived from this vessel supply to the various portions of the hypothalamus.[2]

Despite the consequences, the long-term effects of aneurysmal SAH on hypothalamic–pituitary function have received little systematic attention. Further, discrepant results have been reported regarding the incidence of endocrine dysfunction, which have been found to vary widely from 11% to 50%.[3] The pattern of hormonal impairments has been shown to differ substantially, with growth hormone deficiency combined either with corticotrophin (ACTH) or with gonadal dysfunction.[4] Follow-up studies of patients who have survived SAH has shown relatively high rates of functional limitations along with quality-of-life impairment, such as fatigue, decreased mobility, loss of motivation, abnormally low independence, and participation on measures of social functioning.[5]

The cause of these functional problems remains, at least in part, unclear and many of these symptoms are similar to those occurring in patients with untreated hypopituitarism. [4, 5] Based on this, we conducted the study to observe the pattern of pituitary dysfunction in patients with acute phase of subarachnoid haemorrhage, who were admitted in the tertiary care hospital.

Materials and Methods

We performed a prospective, observational study of patients admitted with subarachnoid haemorrhage in the Department of Anesthesiology and critical care medicine Sheri Kashmir institute of Medical Science. The study was conducted after approval from the Institutional Ethical Committee. A total of 98 patients were enrolled in the study.

Demographic data including age and gender were recorded and a detailed clinical examination of all the patients was done and documented including the Glasgow Coma Scale and the vital parameters. The grading and the severity of bleeding seen on brain computed tomography scan was also recorded. All the patients were admitted to the ICU and closely monitored.

Blood samples were collected from all the subjects (between 8:00 and 8:30 AM) for hormone estimation. The hormone assay included serum cortisol, thyroxine (FT_4), tri-iodothyronine (FT_3), thyroid-stimulating hormone (TSH), prolactin (PRL), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone in men and estradiol in women. The assays were performed by electro-Chemilumniscence (ECLIA) using commercial kits in duplicate and according to supplier protocol (Abbott Germany; Siemens USA). The assays were performed on auto-analysers Abbott i1000SRXP and Siemens Advia centaur XP. Serum insulin was measured by Enzyme linked immunosorbent assay (ELISA) using kit supplied by Calbiotech, India. Intra and inter-assay variations were within the limits as specified by manufacturer.

Statistical Analysis

The recorded data was compiled and entered in a spread sheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean±SD and categorical variables were summarized as percentages. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables A P-value of less than 0.05 was considered statistically significant.

Results

Ninety eight patients were included for the present study. The mean age of the patients was 58.3±10.15 years. About 36 % of the patients were in the age group of 55 to 65 years. Sixty seven per cent of the studied patients had GCS ranging from 5/15 to 12/15 and the remaining 33% of the patients had GCS of 13/15 to15/15.

The detailed hormone profile of these patients is shown in table 1. As can be seen from the table 1 nine out of 98 patients (10%) had low TSH values, however their free T4 or T3 were in the normal range. Elevated TSH levels (> 10IU) were detected in 14 (14.3%) patients. Fifty five out of 98 patients (56%) had cortisol level greater than 30.

Twenty five (26%) of 98 patients were females and 13 had low FSH levels. FSH was raised in 2 and they were in post menopause state with age was greater than 60.

In 73 (74.4%) male patients, the mean prolactin levels were 11.80±4.5ng/ml and prolactin level (43 .27±6.10) were increased in 21 male patients and decreased in 4 patient with values <3.15ng/ml.

Table 1: Details of anterior pituitary hormone status in patients with subarachnoid haemorrhage.

Hormone Parameter	mean±S.D (range)	%age of patients with normal level (range)	%age of patients with elevated level (range)	%age of patients low level (range)
TSH (µ IU/ml)	5.45±3.67 (range)	**86.5**	**10.0**	**3.5**
FT3 (pg/ml)	2.80±0.88 (range)	**98.3**	**0**	**1.7**
FT4 (ng/dl)	1.25±0.50 (range)	**92.5**	**0**	**7.5**
Cortisol (µg/dl)	27.38±12.88 (range)	**100**	**0**	**0**
FSH levels (µIU/ml)	10.66±8.92 (range)	**98**	**2**	**0**
LH levels (µIU/ml)	11.18±5.58 (range)	**93**	**4**	**3**
Testosterone((ng/ml)	4.93±2.51 (range)	**80**	**0**	**20**
Estradiol (pg/ml)	31.96±12.51 (range)	**87**	**0**	**13**
Prolactin (ng/ml)	14.20 ±4.5 (range)	**88**	**10**	**2**

Discussion

The present study was undertaken to observe the incidence, pattern, and severity of pituitary endocrine dysfunction after SAH. No reliable criteria are currently available to identify patients who are potentially at higher risk to develop hypopituitarism after SAH. In the present

study we analysed pituitary endocrine function in 98 patients who had SAH and were admitted to the tertiary care centre. We found subclinical hypothyroid in 9 patients with mean TSH levels of 6.16±1.41 µIU/ml. In 4 patients TSH levels were >10 µIU/ml. Our findings were consistent with the study of Ioanna Dimopoulou et al and Julio Leonardo Barbosa Pereira et al who investigated the incidence, pattern and magnitude of neuroendocrine changes in long-term survivors of aneurysmal subarachnoid haemorrhage (SAH).[5-6] They observed thyroid dysfunction in the form of subclinical hypothyroidism in 7% and 9% of their patients, respectively. Parenti G et al also studied the relationship between SAH and anterior pituitary function.[7] Gonadotropins secretion failure represented the most prevalent hormonal deficiencies in 33.3% of their patients. L Khajeh et al also described the occurrence and course of anterior pituitary dysfunction after SAH.[8] Gonadotropin deficiency was most frequently observed in 29 (34%) patients. They observed pituitary dysfunction which persisted until 14 months in 6 (8%) patients and gonadotropin deficiency in 4 (5%) patients.

We also studied the testosterone levels in male patients. The mean testosterone levels were 4.93±2.51ng/ml. Out of 73 male patients, 24 patients were having low testosterone levels.

Out of our 25 female patients, low estradiol was detected in 9 (30.8%) patients. Vladimir Jovanovic et al evaluated pituitary function in 93 SAH survivors. Forty seven of their patients (50.5%) had normal hormone values. One patient had deficiencies of gonadal, adrenal and GH and two patients had deficiency of all pituitary hormones. [9]

We also studied serum prolactin levels in all the patients. In 75 male patients the mean prolactin levels were 11.80±4.5ng/ml (normal range 3.5 to 19.4ng/ml). In 10 patients, the serum prolactin levels were increased with the mean levels of 37.45 ng/ml. In 23 female patients, the mean prolactin levels were 15.20±8.89. No female was detected with abnormal prolactin levels. Similar results were observed by Mangieri et al who studied the hormonal profiles of patients in the hyperacute phase of SAH (the first 24 hours).[10]

The findings were also consistent with Julio Leonardo Barbosa Pereira who observed greater incidence of hormone deficiency in patients with a Glasgow Coma Scale score ≤13 (t test, p=0.008), Hunt-Hess grade ≥4 (t test, p<0.001), or Fisher grade 4 (t test, p=0.039). [11] Hormone deficiency was not significantly associated (p>0.05) with increased hospitalization or worse clinical outcome.

Conclusion

We conclude that that anterior pituitary hormonal deficiency occurs in a substantial number of patients at an initial stage of SAH without any significant during the initial phase. However, the late stage occurrence needs to be studied in detail with long term follow-up and evaluation. Thus, it becomes essential to evaluate these patients continuously on long term with periodic endocrine examination.

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