International Journal of Physical Sciences Vol. 7(14), pp. 2161 - 2165, 30 March, 2012
Available online at http://www.academicjournals.org/IJPS
DOI: 10.5897/IJPS12.031
ISSN 1992 - 1950 ©2012 Academic Journals

Full Length Research Paper

Hematological parameters in idiopathic intracranial hypertension

Suber DİKİCİ[1]*, Anzel BAHADIR[2], Gulsen KOCAMAN[3] and Seyma OZDEM[1]

[1]Department of Neurology, Duzce University, Medical School, Duzce, Turkey.
[2]Department of Biophysics, Duzce University, Medical School, Duzce, Turkey.
[3]Department of Neurology, Bezmi Alem Foundation University, Medical School, Istanbul, Turkey.

Accepted 6 March, 2012

In this study, we investigated the relationship between cerebrospinal fluid (CSF) pressure and hematological parameters in twenty one idiopathic intracranial hypertension (IIH) patients recruited from the patients' records of Duzce University and Bezmialem Foundation University Medical Faculty Hospitals between 2009 and 2011. We carried blood and CSF examinations to exclude other disorders known to cause increased intracranial pressure. The relationship between CSF presssure parameters and hemotological parameters were examined using Pearson correlation coefficient. According to Pearson test, CSF pressure remained significantly associated with platelet distribution width (PDW) (p: 0.041; r: 0.461), having possitive correlation at moderate level and with red cell distribution width (RDW) (p<0.0001; r: 0.721), having positive correlation at stronger level (Figure 2). Additionaly, CSF pressure was found negatively related with mean corpuscular volume (MCV) (p: 0.017; r: -0.525), with mean corpuscular hemoglobin (MCH) (p: 0.015; r: -0.535) and with mean corpuscular hemoglobin concentration (MCHC) (p: 0.038; r: -0.468) at stronger level. We suggest the investigation of the relation between the hematologic parameters to cerebral blood flow is an important task to uncover the veil of the mystery behind etiopathogenesis of IIH.

Key words: Headache, hematological parameters, idiopathic intracranial hypertension, pseudotumor cerebri, cerebrospinal fluid pressure.

INTRODUCTION

Pseudotumor cerebri (PTC) is a condition of increased intracranial pressure (ICP) and papilledema without a mass lesion, hydrocephalus, focal structural, biochemical and cytological abnormality. The disorder of PTC is also alternatively known as ‘‘idiopathic intracranial hypertension (IIH)’’ (Wall, 1991; Kesler and Fattal-Valevski, 2002). The symptoms of headaches and visual disturbances are the most common manifestations of the disease. The incidence of PTC in the general population is around 1:100.000, whereas in obese women aged 15 to 44 years, the incidence rate is 10 to 20: 100.000 (Ivancic and Pfadenhaur, 2004; Durcan et al., 1988). The“International Headache Society's (IHS)” defines the criteria for idiopathic intracranial hypertension (IIH) as follows (IHS Classification, 2004):

1. Alert patient with neurological examination are either normal or demonstrates any of the following abnormalities:

(a) Papilledema
(b) Enlarged blind spot
(c) Visual field defect (progressive if untreated)
(d) Sixth nerve palsy

2. Increased cerebrospinal fluid (CSF) pressure (>200 mm H_2O in non-obese patients, >250 mm H_2O in obese patients) measured by lumbar puncture in the recumbent position or by epidural or intraventricular pressure monitoring.
3. Normal CSF chemistry (low CSF protein is acceptable) and cellularity.

*Corresponding author. E-mail: suberdikici@gmail.com. Tel: +90 505 5657606. Fax: + 90 380 5421302.

4. Intracranial disease (including venous sinus thrombosis) ruled out by appropriate investigation.
5. No metabolic, toxic or hormonal cause of intracranial hypertension.

The most common symptom is headache. The other less frequent symptoms are transient visual obscuration, tinnitus and diplopia (Giuseffi et al., 1991). The etiology and pathogenesis of PTC are still not fully understood. Several different hypotheses formed by excess of CSF production, CSF outflow reduction, incresed brain water content, obstruction to venous outflow and increased cerebral blood volume had been proposed for the etiopathogenesis of PTC (Spennato et al., 2011). In this study, we investigated the relation of CSF pressure to hematological parameters in PTC patients.

MATERIALS AND METHODS

We included 21 patients with IIH recruited from the patients' records of Duzce University and Bezmialem Foundation University Medical Faculty Hospitals between 2009 and 2011. We took Dandy criteria as a reference for this joint study (Dandy, 1937). We collected data for age, obesity, presence of papilledema, comorbidities, radiographic findings, laboratory findings and treatments. All patients were made to undergo blood and CSF examinations to exclude other disorders known to cause increased intracranial pressure. They all had brain computed tomography (CT) or magnetic resonance imaging (MRI) investigations.

The following hematological parameters were studied: Hemoglobin (Hb), hematocrit (Hct), red blood cell (RBC), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), red cell distribution width (RDW), white blood cell (WBC), platelet count (PLT), mean platelet volume (MPV) and platelet distribution width (PDW). The blood samples were taken before the measurement of CSF pressure. The general procedure for measurement of CSF pressure was applied to all patients and composed of lumbar puncture included draining of the CSF with a 22 G atraumatic needle between 3rd and 4th dorsal processes of the lumbar vertebrae in a supine position. The volume of the drained CSF was between 10 and 20 ml.

Statistical analysis was performed using SPSS (SPSS for Windows version 11.5, USA). The relationship between CSF presssure parameters and hemotological parameters were examined using Pearson correlation coefficient. The significance level was set at $P<0.05$. Moreover, a multivariate analysis was carried out to identify the independent predictors of increase in CSF pressure.

RESULTS

The study composed of 21 patients (16 female, 5 male) with IIH. The mean age and limits for the age of the patients were 34.2±10.2 years and 18 to 52 years respectively. The average body mass index was 32.6 ±8.7 kg/m^2 and the range 22 to 52 kg/m^2. Eleven of them were obese. Thirteen of the patients was reported to be smoker.

The most common symptom in our patients was headache (85.7%). The other symptoms were blurred vision (66.7 %), loss of visual acquity (28.6 %), nausea (28.6 %), diplopia (23.8 %), photopsia (14.3%) and tinnitus (9.5%). Sixteen patients (76.2%) had papilledema related to the diagnosis IIH. When the CSF pressure was taken into consideration, it ranged from 250 to 940 mm H_2O with a mean value of 413.3±201.1 mm H_2O. The statistical analysis demonstrated that the CSF pressure did not correlate with the papilledema.

The potential etiologic factors including adrenal or parathyroidal abnormalities, use of estrogen, cortisol, tetracycline, vitamin A and nalidixic acid, presence of sepsis for IIH were excluded. All patients were treated with acetazolamide. Six patients took corticosteroids and five patients topiramate in addition to acetazolamide. There were no treatment-related complications in our study.

Pearson correlation analysis revelaed positive strong (r:0.554), but non-significant (p:0.11) correlation between RDW and PDW, and positive strong (r:0.747) significant (p:0.000) correlation between RDW and MPV. In addition, a strong negative significant correlation between RDW and hematocrit (r: -0.676; p: 0.001), MCV (r: -0.863; p: 0.000), MCH (r: -0.890; p: 0.000), MCHC (r: -0.764; p: 0.000) were found in analysis. A strong positive significant correlation was found between PDW and MPV (r: 0.665; p: 0.001). A moderate negative, but non-significant correlation were found between PDW and hematocrit (r: -0.472; p: 0.036), MCHC (r: -0.528; p: 0.017). Although, the correlation between MPV and MCV (r: -0.667; p:0.001), MCH (r: -0.723; p:0.000), MCHC (r: -0.729; p: 0.000) were strong negative significant, a strong negative, but non-significant correlation was found between MPV and hematocrit (r: -0.588; p:0.06). The correlation between thrombocyte number and leucocyte number was found to be strong positive, but non-significant (r: 0.565; p: 0.009) in our analysis.

The Pearson correlation analysis showed that the CSF pressure correlated with hematological parameters. According to this test, CSF pressure remained significantly associated with RDW ($p<0.0001$; r: 0.721) having positive correlation at stronger level (Figure 1) and with PDW (p: 0.041; r: 0.461) having possitive correlation at moderate level (Figure 2). Furthermore, CSF pressure was significantly associated with RDW ($p<0.0001$; r: 0.721) having possitive correlation at stronger level (Figure 2). Additionaly, CSF pressure was found negatively related with MCV (p: 0.017; r: -0.525), with MCH (p: 0.015; r: -0.535), and with MCHC (p: 0.038; r: -0.468) at stronger level.

DISCUSSION

The pathogenesis, cilinical and radiologic findings, and treatment of PTC or IIH still have dark areas needed to be enlightened. In addition, the relation IIH with

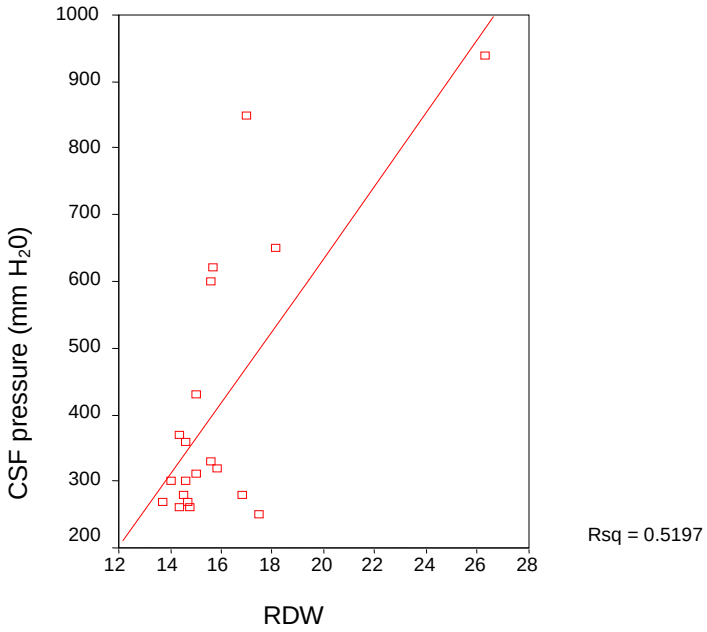

Figure 1. Scattergram showing the correlation between CSF and RDW.

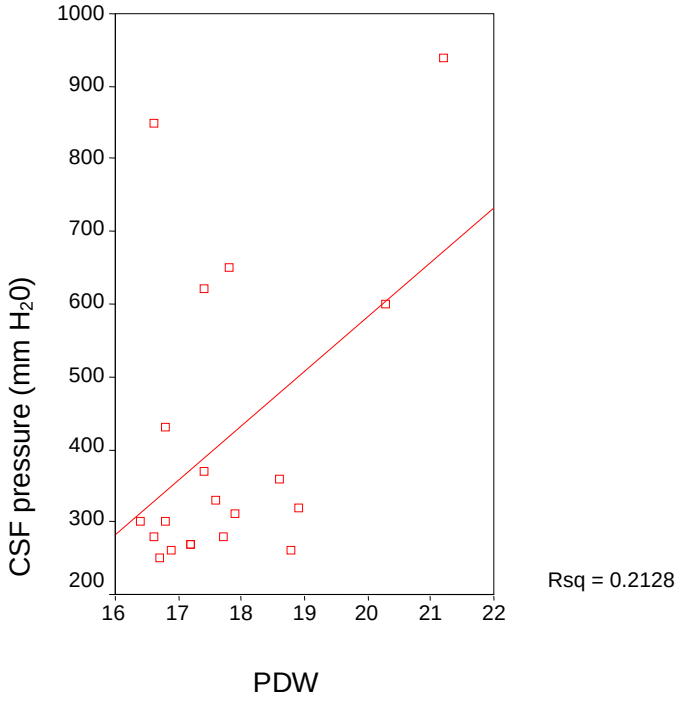

Figure 2. Scattergram showing the correlation between CSF and PDW.

hematologic parameters have not been stuided up to now. The headache without papiledema was the chief complaint of five patients in presentation to the hospital. Given the fact that the headache may be the sole symptom of IIH, we should always take IIH as a potential etiology into the differential diagnosis of headache in the hospital setting. The obesity-related risk was much more pronounced for female patients than it was for male

patients (Kesler et al., 2001; Celebisoy et al., 2002).

The changes in CSF in patients with IIH have been studied by many authors. In spite of abundant findings in extensive researches, IIH still keeps its mystery about its etiopathogenesis. Some authors postulated that significant increase in CSF might be due to a primary failure of autoregulation in IIH. Gjerris et al. (1985) indicated that increased cerebral blood flow would alter the intracranial volume-pressure relationship and interfere with CSF absorption. In a study by Bateman (2004) the mean of total CSF values in IIH patients were found to be greater than it were found in the control group using MR flow quantification and MR venography. Lorberboym et al. (2001) also reported that the correlation between reduced cerebral blood flow (CBF) and IIH disease severity were significant determined by photon emission computed tomography. Bicakci et al. (2006) reported that, although CBF decrease was statistically significant, finding for the development of IIH and CBF increase was found to have non-significant effect on development of IIH. On the contrary, by using positron emission tomo-graphy, Brooks et al. (1985) stated that, any deterioration in cerebral hemodynamics is not associated with significant increase in CSF pressure of IIH patients.

There is no comprehensive study investigating the relation of the findings of PTC patients to hematologic data up to now in the literature. Red cell size variation distribution is measured by the RDW and it is given by the degree of anisocytosis (Kotila, 2006). This parameter is basic for distinguishing between iron deficiency and β-thalassemia trait (Bessman et al., 1983). Walid et al. noticed that twelve out of 23 PTC patients had high RDW and 10 out of 20 patients had papilledema (Walid et al., 2011). The most frightening complications of PTC are optic nerve edema and loss of vision. Retinopathy is a frequent finding in anemic and thrombocytopenic patients, although it is often not significant clinically. In this context, Carraro et al. (2001) reported that retinopathy was observed in 28.3% of the patients as a whole and the presence of fundus lesions was found to be closely related to severe anemia (Hb < 8 g/dL) and severe thrombocytopenia (PLT < 50 x 10^9/L). In addition, in this study, the data of age, low Hgb levels, PLT counts, RDW-CV and increased MCV, MPV and P-LCR were all significantly associated with the presence of fundus lesions at univariate analysis. In our study, we had a patient with high CSF (940 mm H_2O) and severe iron deficiency anemia (RBC: 3.73 K/ul, Hb: 5.58 g/dl, Hct: 5.58%, MCV: 53.9 fL, MCH:15.0 pg, RDW: 26.3%). Firteen patients had iron deficiency anemia with the findings of low MCV (< 86 ±10 fl) and high RDW (>12.8±1.2 %) values. The remaining patients have not had any hematologic abnormality. The most remarkable finding in our study was the positive significant relation between CSP pressure and RDW.

PDW is a measure of platelet anisocytosis. The PDW has been found to be useful in distinguishing between essential thrombocythaemia and reactive thrombocytosis. Although, PDW is increased in essential thrombocythemia, PDW is normal in reactive thrombosytosis (Kotila, 2006). Additionally, the determination of the PDW reference range is fundamental, and the association of this parameter with the platelet number and MPV may be used for the diagnosis and differentiation of several pathologies (Farias et al., 2010). In an article by Wiwanitkit (2004), it was reported that significant correlation is present between PDW and RDW. He claimed that the anisocytosis of red blood cells and platelets might co-occur. But these data are basic observations; further in-depth evaluation of the platelet parameters is recommended. According to the data of our study, although there was no positive strong correlation between PDW and RDW, we found a positive strong and significant correlation between RDW and MPV. In addition, an important finding of our study was the presence of moderate positive correlation between CSF pressure and PDW.

The pathogenesis of IIH is still unknown and different mechanisms have been suggested that including increase in CSF production, reduced absorption of CSF or systemic venous hypertension. In the context that, IIH as a peculiar clinical syndrome of cerebral venous thrombosis has been proposed on the essential of surveys showing an increased rate of coagulation abnormalities in patients with IIH (Agostoni and Aliprandi, 2009; Backhouse et al., 2001). Our study revealed a strong positive and significant correlation between RDW and MPV, and a moderate negative and non-significant correlation between PDW and hematocrit values.

In conclusion, the correlation analysis within the hematologic variables (RDW, PDW, MPV, MCV, MCH, MCHC, Hct) and between the hematologic data and the determinants of cerebral hemodynamic including cerebral blood flow and volume values are of great importance for contributing to the delineation of IIH etiopathogenesis. Because, severe anemia, thrombocytosis and anicocytosis are thought to play important role in the development of IIH. The importance of hemodynamics in the cranial system signifies that studies have been performed on the identifaction of intracranial pressure pulses and the cerebral blood flow velocity of the morphological structure (Mokri, 2001; Hu et al., 2010; Kim et al., 2011). In this context, although there is a long way to compare estimates and draw clear-cut conclusions, we think the investigation of the relationship between hematologic parameters and cerebral blood flow has an important task to uncover the veil of mystery on etiopathogenesis of IIH.

REFERENCES

Agostoni E, Aliprandi A (2009). Alteration in the cerebral venous as a cause of headache. Neurol. Sci., 30(1):7-10.

Backhouse OC, Johnson M, Jamieson DR, Menage MJ, Goulding PJ, McVerry BA, Cawthray N (2001). Familial thrombophilia and idiopathic intracranial hypertension. J. Neuroophthalmol., 25(3):135-141.

Bateman GA (2004). Idiopathic intracranial hypertension: priapism of the brain? Med. Hypothese. 63(3): 549-552.
Bessman JD, Gilmer PR, Gardner FH (1983). Improved classification of anaemias by MCV and RDW. Am. J. Clin. Pathol., 80 (3):322-326.
Bicakci K, Bicakci S, Aksungur E (2006). Perfussion and diffusion magnetic resonance imaging in idiopathic intracranial hypertension. Acta Neurol. Scand., 114(3):193-197.
Brooks DJ, Beaney RP, Leenders KL, Marshall J, Thomas DJ, Jones T (1985). Regional cerebral oxygen utilization, blood flow and blood volume in benign intracranial hypertension studied by positron emission tomography. Neurology, 35 (7): 1030-1034.
Carraro MC, Rossetti L, Gerli GC (2001). Prevalence of retinopathy in patients with anemia or thrombocytopenia. Eur. J. Haematol., 67(4): 238-244.
Celebisoy N, Secil Y, Akyurekli O (2002). Pseudotumor cerebri: etiological factors, presenting features and prognosis in the western part of Turkey. Acta Neurol. Scand., 106(6): 367-370.
Dandy W (1937). Intracranial pressure without brain tumor. Ann. Surg., 106(4): 492-513.
Durcan FJ, Corbett JJ, Wall M (1988). The incidence of pseudotumor cerebri: Population studies in Iowa and Louisiana. Arch. Neurol., 45 (8):875-877.
Farias MG, Schunck EG, Dal Bó S, de Castro SM (2010). Definition of reference ranges for the platelet distribution width (PDW): a local need. Clin. Chem. Lab. Med., 48(2): 255-257.
Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991). Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): a case-control study. Neurology, 41(2):239–244.
Gjerris F, Soelber G, Sorensen P, Vorstrup S, Paulson OB (1985). Intracranial pressure, conductance to cerebrospinal fluid outflow and cerebral blood flow in patients with benign intracranial hypertension (Pseudotumor cerebri). Ann. Neurol., 17(2):158-162.
Hu X, Glenn T, Scalzo F, Bergsneider M, Sarkiss C, Martin N, Vespa P (2010). Intracranial pressure pulse morphological features improved detection of decreased cerebral blood flow. Physiol. Meas., 31(5): 679-695.
Ivancic R, Pfadenhaur K (2004). Pseudotumor cerebri after hormonal emergency contraception. Eur. Neurol., 52(2):120.
Kesler A, Fattal-Valevski A (2002). Idiopathic intracranial hypertension in the pediatric population. J. Child. Neurol., 17(10):745-748.
Kesler A, Goldhammer Y, Gadoth N (2001). Do men with idiopathic intracranial pressures share the same characteristics as women? A retrospective review of 141 cases. J. Neuroophthalmol., 21(1):15–17.
Kim S, Hu X, McArthur D, Hamilton R, Bergsneider M, Glenn T, Martin N, Vespa P (2011). Inter-subject correlation exists between morphological metrics of cerebral blood flow velocity and intracranial pressure pulses. Neurocrit. Care, 14(2):229-237.
Kotila TR (2006). Automated techniques in hematology. Niger. J. Med.15(1):30-33.
Lorberboym M, Lampl Y, Kesler A, Sadeh M, Gadot N (2001). Benign intracranial hypertension: correlation of cerebral blood flow with disease severity. Clin. Neurol. Neurosurg. 103 (1): 33-36.
Mokri B (2001). The Monro-Kellie hypothesis: applications in CSF volume depletion. Neurology, 56(12):1746–1748.
Spennato P, Ruggiero C, Parlato RS, Maria Consiglio- Buonocore M, Varone A, Cianciulli E, Cinalli G (2011). Pseudotumor cerebri. Childs Nerv. Syst. 27(2):215-235.
The International Classification of Headache Disorders (2004). 2nd edition. Cephalalgia. 24 (Suppl. 1): 9–160.
Walid MS, Sanoufa M, Robinson JS III, Boltia MC, Robinson JE (2011). Pseudotumor Cerebri: Categorical Disease or Spectrum of Disease. J. Neurol. Res., 1(1): 6-10.
Wall M (1991). Idiopathic intracranial hypertension. Neurol. Clin., 9(1): 73-95.
Wiwanitkit V (2004). Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clin. Appl. Thromb. Hemost., 10 (2):175-178.