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LEVELS OF ANTIPHOSPHOLIPID ANTIBODY, ERYTHROCYTE SEDIMENTATION RATE AND PLATELETS AMONGST MIGRAINE PATIENTS IN NORTH-EASTERN, NIGERIA

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ABSTRACT
Migraine is mostly mis-diagnosed, and even when correctly diagnosed does not receive desired attention. This study was aimed at assessing the levels of antiphospholipid antibody, erythrocyte sedimentation rate and platelets during migraine attack so as to provide physicians and allied healthcare professionals with guidelines for the diagnosis and subsequent management of migraine in clinical practice. One hundred consecutive adult (18 years and above) patients that met the International Headache Society diagnostic criteria for migraine who attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital, Maiduguri from May, 2009 to December, 2010 and from whom informed consent was obtained were evaluated for this disorder. General, physical and neurological examinations were also conducted. Samples were taken for haematological and immunological analyses before and after acute therapy. Acute migraine attack caused a statistical significant increase in the levels of antiphospholipid antibody, erythrocyte sedimentation rate and platelets among the migraineurs studied ($p<0.001$). Acute migraine therapy significantly reduced the levels of laboratory parameters studied among migraineurs with either moderate or severe attack ($p<0.001$). Based on this study, acute migraine attack was found to increase the levels of antiphospholipid antibody, erythrocyte sedimentation rate and platelets above hospital reference value and acute therapy was able to significantly reduce their levels. It is suggested that antiphospholipid antibody, erythrocyte sedimentation rate and platelets should be included as a marker for migraine detection.
Keywords: Migraine, Antiphospholipid antibody, Erythrocyte sedimentation rate, Platelets

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INTRODUCTION

Globally migraine disorder is among the most prevalent, recurrent and disabling of all neurovascular illnesses[1]. Several literature reports on migraine headache[2-5] showed that only about one-half of migraineurs are properly diagnosed; and of these, about one-half receive prescription drugs or treatment in the developed countries. The situation is even worse in most developing countries[5,6,7] in which less than 5% are properly diagnosed and about a quarter receive treatment. Antiphospholipid antibody (APA) has occasionally been observed in patients with transient neurologic symptoms including migraine[8-10] although Rachel et al[11] reported a lack of association between APA and acute migraine attack. APA can also be found in the blood of individuals without any disease process[11]. Harmless APA can be detected in the blood for a brief period occasionally in association with variety of conditions, including bacterial, viral and parasitic infections. Certain drugs can cause APA to be produced in the blood, including some antibiotics, cocaine, hydralazine, procainamide and quinine[12]. The apparent increase in the interleukin (IL) 4 and IL-5 cytokine profile observed during the acute migraine attack leads to speculation that a preferential enhancement of T_H2-type cytokine production may contribute to the pathogenesis of migraine[13]. The evidence now available suggests an involvement of platelets in migraine pathogenesis[14-17]. In comparison with normal control subjects, migraine sufferers have shown higher levels of platelets circulating micro-aggregates during attacks and in prodromal periods[18]. Andrea et al[19] reported that patients

suffering from classic migraine showed an extremely high incidence of platelet activation (greater than 90% of cases studied), when compared with common migraine sufferers (33% of patients). Migraine and headache beginning after 50 years of age require checks for Erythrocyte Sedimentation Rate (ESR) as possible work-up[17]. To the best of our knowledge no study was carried out in our community that focuses on the involvement of APA, ESR and platelets in migraine. Therefore, this study was embarked upon in order to assess the levels of APA, ESR and platelets in migraine attack.

MATERIALS AND METHODS

From May, 2009 to December, 2010, one hundred consecutive adult migraine patients that attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital (UMTH), Maiduguri were prospectively studied with their consents. The study was approved by the Research and Ethics committee of UMTH. Pregnant women, patients with clinical evidence of an organic disease known to cause migraine and those that have a socioeconomic factor (culture and poverty) were excluded. Personal interviews using a structured questionnaire were conducted individually with the 100 patients. General, physical and neurological examinations were also conducted. Samples were taken for haematological and immunological analyses before and after acute therapy on every study subject. Those patients that did not meet the inclusion criteria were given analgesics and were not enrolled for the study.

Antiphospholipid antibody (APA): APA was determined using the serum of 3 ml blood collected from each study patient. The procedure has three phases. In phase one the patient's sample was calibrated, controlled, prediluted and pipetted into the wells of a microplate. This was then incubated for 30 mins and was later washed with a phosphate buffer (pH of 7.4) (which is use for removing non-reactive serum components). In the second phase, anti-human IgG or anti-human IgM horseradish peroxidase conjugate solution was pipetted into the wells of the microplate to recognize IgG class autoantibodies or IgM, class autoantibodies bonded to the immobilized antigens. After 15 mins incubation, all the excess enzyme conjugates which was not specifically bonded was washed away with wash (phosphate) buffer. Finally, a chromogenic substrate solution containing TMB (3, 3, 5-tetramethyl benzidine) was dispensed into the wells and incubated for 15 mins after which the colour of the solution changed to blue. Colour development was stopped by the addition of 1ml HCl acid as a stop solution and the colour of the solution was changed to yellow. The amount of colour is directly proportional to the concentration of IgG and IgM antibodies present in the original sample. A microplate reader with a 450 nm filter was used in reading the optical density. A biochromatic measurement with 600 - 610 nm was used as a reference. The UMTH reference value for APA is $\leq$ 20 IU/ml.

Erythrocyte sedimentation rate (ESR) (Westergren Method): Blood (2 ml) was mixed with 0.5 ml of sodium citrate anticoagulant and a standard clean dry westergren tube was filled to zero mark. The tube was then placed in vertical position on a flat bench away from sunlight, dust and vibration. The level of the exposed plasma was read at 1 h (i.e. the distance of the surface meniscus of the plasma to the top of the column of sedimentation of red cells in millimetre). The UMTH reference value for ESR is 0 - 10 mm/h.

Platelets count: Zero point three eight milliliters (0.38 ml) of 1% Ammonium oxalate diluting fluid was measured and dispensed into a tube. Twenty microlitres (0.02 ml) of EDTA blood sample was added, mixed and allowed to stand for 5 mins. The counting chamber was charged with the sample and was allowed to stand undisturbed for 20 mins. The chamber was placed in a petri dish containing a dampened blotting paper and covered to prevent the fluid from drying. This was then placed on the light microscope (AXIOSKOP 40) stage and using x10 objective lens the ruling of the grid was focused, thus bringing the central square of the chamber into view. The x40 objective lens was used in focusing the small platelets and was counted in the small 5 squares of the chamber. Platelets counted (per litre) = platelet cells counted x 20 x 10^6 / 0.2 x 0.1; where 20 is the dilution factor, 0.2 mm is the area counted and 0.1 mm is the depth of the chamber. The UMTH reference value for platelets is 150 - 400 x 10^9/L.

Statistical analyses: the data was analyzed using statistical analysis software (SAS) system version 16. Student t-test was used to determine significance of association between non-categorical variables. P values less than 0.05 were considered significant, less than 0.01 highly significant and less than 0.001 very significant.

RESULT

The mean ± SD before and after treatment among migraineurs with moderate headache showed that APA, ESR and Platelets were 20.4 ± 13.4; 7.7 ± 4.4, 18.6 ± 8.5; 4.5 ± 2.4 and 364.0 ± 130.0; 172.0 ± 46.0 respectively. Migraineurs with severe headache had their mean ± S.D before and after treatment for APA, ESR and platelets as 33.4 ± 14.9; 8.9 ± 4.7, 18.8 ± 9.4; 4.9 ± 2.7 and 414.0 ± 144.0; 185.0 ± 61.0 and respectively (Table 1). There was a significant increase in the levels of ESR and platelets among migraine

patients studied with moderate and severe migraine ($p<0.001$). The levels of APA among migraineurs with severe attack significantly increased ($p<0.001$), whereas those with moderate attack did not had their APA increased. The increase in the levels of ESR and platelets among migraineurs with moderate and severe migraine did not differ significantly ($p>0.05$), but migraine patients with severe attack had higher APA levels than those patients with moderate attack ($p<0.001$). Acute therapy with sumatriptan and Cafergot® tablets were able to cause a significant reduction in the levels of APA, ESR and platelets among migraineurs studied ($p<0.001$) (Table 1).

DISCUSSION

The significant increase in the levels of antiphospholipid antibodies (APA), ESR and platelets among migraineurs with acute attack in this study ($p<0.001$) agrees with most literature reports in which their levels were also found to be significantly higher among the study subjects[8,11,16,17]. Rachel et al[11] has suggested that APA should be included as a marker for migraine detection in susceptible individuals. However these findings did not agree with the report of William[12] in which the APA was found to be present in the blood of some individuals without migraine and some other related disease process. The latter finding could be as a result of certain drugs including antibiotics, stimulants, hydrallazine, procainamide and quinine that may elevate the APA's level[12]. The increase in the levels of ESR and platelets during severe migraine attack did not differ significantly from those having moderate attack. However, migraine patients with severe attack had higher APA levels than those with moderate attack ($p<0.001$). This finding slightly differs from the report of Rachel et al[11] in which the increase in the levels of ESR, platelets and APA were not different among patients with either moderate or severe migraine attack. A significant reduction in the levels of ESR ($p<0.001$), platelets ($p<0.001$) and APA ($p<0.001$) among studied migraineurs following acute therapy with sumatriptan or Cafergot® tablet observed in this study agrees with several reports in which the levels of these laboratory parameters were significantly reduced following acute therapy[8,11,20].

CONCLUSION

Acute migraine attack significantly increased the levels of APA, ESR and Platelets among migraineurs studied and acute therapy was able to cause a significant reduction in their levels. Despite abnormal increase in the levels of these laboratory parameters in the blood of some individuals without migraine, it is recommended that they should be included as a marker for detecting migraine in susceptible individuals.

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TABLE 1: LEVELS OF ANTIPHOSPHOLIPID ANTIBODY, ERYTHROCYTE SEDIMENTATION RATE AND PLATELETS

Laboratory Parameters	Reference value (RF)	Severity of migraine attack	Mean ± SD		P-value
			Before therapy	After therapy	
APA	20 IU/L	Moderate	20.4±13.4 ^{APMB}	7.7±4.4	0.000*
		Severe	33.4±14.9 ^{APSB}	8.9±4.7	0.000*
ESR	0-10 mm/h	Moderate	18.6±8.5 ^{EMB}	4.5±2.4	0.000*
		Severe	18.8±9.4 ^{ESB}	4.9±2.7	0.000*
Platelets	150-400 x 10^9/L	Moderate	364.0±130.0 ^{PMB}	172.0±46.0	0.000*
		Severe	414.0±144.0 ^{PSB}	185.0±61.0	0.000*

Moderate, N = 48; Severe, N = 52 RF & EMB (p<0.001) RF & ESB (p<0.001) RF & PMB (p<0.001) RF & PSB (p<0.001) APMB & APSB (p<0.001) EMB = Moderate ESR before therapy ESB = Severe ESR before therapy PMB = Moderate Platelets before therapy PSB = Severe platelets before therapy APMB = Moderate antiphospholipid antibody before therapy APSB = Severe antiphospholipid antibody before therapy SD = standard deviation * = Significant p-value (p<0.05) (Student't' test) APA = Antiphospholipid antibody ESR = Erythrocyte sedimentation rate

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