Abstracts

Altered Matrix Metalloproteinase Dynamics plays a Role in Differential Pathogenesis among Adult Severe Dengue Cases

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INTRODUCTION

Plasma leakage is a pathological hallmark of dengue hemorrhagic fever and dengue shock syndrome. Macrophages are sites for dengue virus (DENV) replication. Matrix metalloproteinases (MMPs) are secreted by macrophages. They degrade extracellular matrix. Balance between MMPs and tissue inhibitors of metalloproteinases (TIMPs; endogenous MMP inhibitor) is critical in plasma leakage in DENV infection.

AIMS AND OBJECTIVES

To assess circulating levels of MMP-9, MMP-13, and TIMP-1 at various clinical stages of DENV infection and look for any association with severity of disease.

MATERIALS AND METHODS

Serum MMP-9, MMP-13, and TIMP-1 (enzyme-linked immunosorbent assay) and routine hematological and biochemical parameters were measured in blood samples (collected thrice during febrile stage, defervescence, and early convalescence) from 48 dengue fever and 20 other febrile illness (OFI) cases (who acted as controls). Cases were classified into severe and nonsevere groups in accordance with clinical data (World Health Organization guidelines, 2009).

RESULTS

The MMP-9 serum levels were significantly lower in dengue compared with OFI during acute febrile stage. The MMP-9 levels of dengue cases correlated positively and MMP-13 negatively with total leukocyte count (TLC). In contrast, MMP-13 positively correlated with serum aspartate transaminase. The TIMP-1 serum levels were significantly higher among severe dengue cases compared with nonsevere cases. Serum TIMP-1 correlated positively with blood urea and serum creatinine levels and negatively with serum albumin among severe dengue cases. The MMP-9/TIMP-1 ratio correlated positively with TLC among nonsevere cases. There was a significant progressive rise in TIMP-1 during the course of dengue; MMP-9 exhibited progressive fall among severe dengue cases in contrast to a significant progressive rise among nonsevere cases.

CONCLUSION

Lower MMP-9 sera levels in dengue cases compared with OFI suggest alterations in MMP dynamics in DENV infection. Significantly higher TIMP-1 in severe dengue cases and differential trend of MMP-9 during the course of dengue among severe and nonsevere cases indicate that balance between these molecules is one of the key regulators of severity in DENV infection, thus strengthening their cases as future potential prognostic markers.

Relationship of Follicle-stimulating Hormone and Follicle-stimulating Hormone Receptor Polymorphism in Women with Unexplained Infertility

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INTRODUCTION

Unexplained infertility is the failure to conceive in a couple for whom no definitive cause for infertility is found. For the female reproductive system to function properly, there has to be a balanced interaction between the hypothalamus, anterior pituitary, and ovaries. Follicle-stimulating hormone (FSH) is released from the anterior pituitary and binds to the FSH receptor (FSHR) on the granulosa cells of the ovary and stimulates the developing follicles in the ovary. Therefore, FSHR plays an integral part in the proper functioning of FSH. Any alteration in the receptor or FSH can lead to infertility. The effect of FSH on the ovary is affected

by the polymorphism of the FSHR gene. Polymorphism at position 680 affects the sensitivity of FSH to its receptor. Clinical studies have demonstrated that Ser680Asn determines the ovarian response to FSH stimulation in patients undergoing *in vitro* fertilization. This study aims at identifying FSHR gene (Ser680Asn) polymorphism in women with unexplained infertility and to study the association between serum FSH and the FSHR gene (Ser680Asn) polymorphism in women with unexplained infertility and controls. A total of 50 women diagnosed with unexplained infertility were enrolled as cases. These were age matched with 50 healthy fertile women volunteers. The distribution of GG genotype was found to be higher in cases as compared with controls. In cases, FSH was found to be higher in GG genotype as compared with AG and AA. To conclude, the high FSH levels in GG genotype is suggestive of resistance of the receptor to FSH.

Evaluating the Role of Testosterone and Estradiol in Men with Acute Ischemic Stroke

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INTRODUCTION

One intriguing aspect of stroke is its higher incidence in men compared with women. Endogenous sex hormones, testosterone and estradiol, may be responsible for this difference.

AIMS AND OBJECTIVES

To study serum testosterone and estradiol levels in men with acute ischemic stroke and to correlate these levels with National Institutes of Health Stroke (NIHS) scale and infarct size in computed tomography (CT).

MATERIALS AND METHODS

A total of 100 male patients with acute ischemic stroke and 100 age-matched controls were included in this case–control study. Patients with hemorrhagic stroke, taking hormonal preparations, or suffering from chronic illness like tuberculosis, cancer, etc., were excluded. Complete history was obtained including presence of established risk factors, and physical examination was done in cases and controls with informed written consent. Severity of stroke in cases was measured by the NIHS scale. A CT scan of the brain was performed within 72 hours of patients' admission to hospital. The infarct size was measured in centimeters as the largest visible diameter of the infarct on CT scan. Fasting blood samples were obtained for routine investigations and estimating estradiol and testosterone levels.

RESULTS

Mean total testosterone level in cases (223.30 ± 143.44 ng/dL) was significantly lower than that of controls (515.34 ± 172.11 ng/dL; $p < 0.001$), while estradiol levels had no significant statistical difference ($p = 0.26$). A significant inverse correlation was found between total testosterone levels and stroke severity ($r = -0.581$, $p < 0.001$) and, also, total testosterone levels and infarct size ($r = -0.557$, $p < 0.001$). Estradiol levels in patients had no significant correlation with stroke severity ($p = 0.618$) or infarct size ($p = 0.463$).

CONCLUSION

Low testosterone levels are associated with increased stroke severity and infarct size in men. Further studies are required to establish whether low testosterone is a cause or effect of ischemic stroke and also to explore the potential benefits of testosterone supplementation in men with acute ischemic stroke.

Assessment of Analytical Performance of Glucose Meter in Pediatric Age Group at a Tertiary Care Referral Hospital

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INTRODUCTION

Glucometers are excellent tools for self-monitoring of blood glucose. They are important especially in circumstances where continuous monitoring is mandatory and at decision-making levels. Tight glycemic control protocols are important for preventing

the ill effects of fluctuating glucose levels. This increases the use of glucometers in various health care settings. As technology advances, glucometers are getting better in terms of quality of results. But still some lacunae are there. We therefore decided to study the quality of glucose meter results in terms of clinical outcomes.

MATERIALS AND METHODS

The present study was conducted in a tertiary care referral hospital. A total of 125 patients were recruited from pediatric wards. Bland–Altman plot, Parkes error grid, and surveillance error grid analysis were used for comparing the results of glucose meter with that of standard laboratory method.

RESULTS

It is found that there is significant difference between the results by two methods. Though minimal, glucose meter results deviate from the results of standard lab method. This will affect the overall patient care, especially in emergency conditions. Sometimes, the risk may be so high that patients may be mislabeled as hypoglycemic when actually they are hyperglycemic and vice versa.

CONCLUSION

This study is the first of its kind as no similar studies have been reported in the pediatric population. For effective use of glucose meter, it should give as accurate as possible estimate of actual glucose levels. Results should not only be accurate but also precise, without which critical errors may be possible. We recommend that for any glucose meter regular maintenance as well as calibration need to be done so that agreement with reference laboratory method is maintained and effective medical decisions are made.

Transcobalamin II Gene Variant 776C>G: Association with Serum Homocysteine Levels and Stroke

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INTRODUCTION

Transcobalamin II (TCN2) protein is solely responsible for the intracellular delivery of vitamin B12. So, genetic variation in TCN2 gene may alter the structure of protein in such a way that could affect its binding affinity to vitamin B12 or its recognition by the cellular receptor, thereby lowering intracellular vitamin B12. Since vitamin B12 is an essential coenzyme for homocysteine remethylation, its deficiency could lead to homocysteine accumulation, a risk factor for stroke.

AIMS AND OBJECTIVES

To explore the association of TCN2 gene polymorphism 776C>G with homocysteine levels and susceptibility to stroke, if any.

MATERIALS AND METHODS

A case–control study was conducted in the Department of Biochemistry and Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India, which included 84 diagnosed cases of stroke and 70 healthy controls. The genotyping for TCN2 776C>G single-nucleotide polymorphism (SNP) was done by polymerase chain reaction restriction fragment length polymorphism. Biochemical assay for serum vitamin B12 was done by enzyme-linked immunosorbent assay and for serum total homocysteine by enzymatic cycling method.

RESULTS

The odds ratio (OR) calculation showed that subjects with GG genotype had 2.5 times higher risk of developing stroke as compared with those with CC genotype (OR = 2.5, 95% confidence interval = 1.063–5.88; p-value < 0.05). The genotype association analysis with median homocysteine levels showed that GG [17.5 (10.2–33) µmol/L] carries a risk for hyperhomocysteinemia as compared with CC [14.2 (10.1–18.8) µmol/L] and CG [14.3 (12.4–24) µmol/L]. However, vitamin B12 level did not vary significantly in GG genotype when compared with the other genotypes.

CONCLUSION

TCN2 gene SNP 776C>G increases the susceptibility to stroke and hyperhomocysteinemia. Thus, this SNP could be a potential candidate to be used for screening patients at risk for stroke and also a target for new drug development. However, our findings are needed to be confirmed by further prospective studies with larger sample size to have substantial evidence.

Frequency of FcγRIIIA-158V/F Polymorphism in Systemic Lupus Erythematosus patients with Lupus Nephritis

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INTRODUCTION

Receptors for immunoglobulin G play a critical role in linking humoral and cellular immune response. The various FcγR genes may contribute to differences in infectious and immune-related diseases in various ethnic populations. Allelic variants of FcγR confer distinct phagocytic capacities, providing a mechanism for heritable susceptibility to immune complex disease. Numerous functionally relevant single-nucleotide polymorphism (SNP) variants and copy number variants (CNVs) have been characterized in the FcγR genes. Many of these variants have also been shown to associate with the risk to development of systemic lupus erythematosus (SLE), and some have been associated with disease progression. In this study, we aimed to investigate whether the distribution of the FcγRIIIA polymorphism determines susceptibility to SLE with lupus nephritis in Indian patients. A total of 32 patients that fulfilled American College of Rheumatology classification criteria for SLE were included in the study. FcγRIIIA genotypes were determined by polymerase chain reaction-based allotyping method with allele-specific primers. The results demonstrated FcγRIIIA-158V/F polymorphism in 91% and FcγRIIIA-158V/V in 9% of the cases. It shows that FcγRIIIA-158 has susceptibility to SLE and lupus nephritis in Indian patients. To our knowledge, this is the first study considering the frequency of FcγRIIIA polymorphism in Indian SLE patients. To enhance our understanding of the functional role of the receptors in SLE, future research will need to integrate the knowledge of SNP and CNV and the functional diversity of the receptors.