



Serum MMP-9 and Malondialdehyde Levels in Nocturnal Enuresis: Exploring Associations and Implications for Adolescent Health"

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Abstract: Enuresis is the most prevalent urologic complaint in paediatric patients and is defined as the involuntary leakage of urine during sleep that happens at least twice per week in children older than 5 years old (or the developmental equivalent) for at least 3 months. The aims of the study were to assess the level of serum MMP-9 and Malondialdehyde (MDA) in children with nocturnal enuresis and to look for a relation between level of metalloproteases and the risk of nocturnal enuresis in adolescence. Methods: 53 patients (10-18 years old) and 47 healthy children were included in the study. Serum MMP-9 were measured in control and cases groups. Results: Nonsignificant difference between studied groups in MMP-9 levels in patient group compared to control group. Conclusions, Nocturnal enuresis were found non difference between studied groups in MMP-9 and MDA levels in cases group compared to control group. More studies are recommended to understand the development of the disease and its prevention.

keywords: Nocturnal enuresis, MMP-9, MDA

1.Introduction

Nocturnal enuresis is known as "nighttime bedwetting in children five years of age or older [1]. Nocturnal enuresis NE can be categorized as primary nocturnal enuresis (PNE) or secondary nocturnal enuresis (SNE) depending on the underlying cause of the condition; additionally, NE can be categorized as monosymptomatic nocturnal enuresis (MNE) or non-monosymptomatic nocturnal enuresis (NMNE) depending on the presence or absence of comorbidities [2]. The most significant factors in an etiology of primary monosymptomatic nocturnal enuresis (PMNE) include nocturnal polyuria, which is linked to inadequate antidiuretic hormone secretion at night, nocturnal detrusor overactivity, and sleep problems. Depending on an etiology, desmopressin, bedwetting alarms, anticholinergics, or occasionally tricyclic antidepressants are used in the treatment of PMNE in children [3]. The extracellular matrix is degraded by matrix

metalloproteinases (MMPs), whose actions are controlled by tissue metalloproteinase inhibitors (TIMPs)[4]. MMPs are a major class of calcium-dependent zinc-containing endopeptidases that are capable to degrade non-matrix proteins including cytokines in addition to extracellular matrix proteins [5].

One of the key signs of periodontal disease is the degradation of extracellular matrix proteins (ECMs) by proteinases, which can come from cellular as well as microbial sources in dental plaque [6]. Previous studies have shown that MMP-1, MMP-2, MMP-3, and MMP-9 are related with bladder cancer and can predict stage, grade, and even the course of the disease [7]. Gelatinase B, also referred to as MMP-9, is a 92 kDa type IV collagenase (EC3.4.24.35). The cysteine sulfhydryl group in the amino-terminal propeptide chelates the zinc in the active site and maintains the latent state of MMP9 in the zymogen, which is synthesised and secreted. Two

primary forms of the latent MMP-9 were discovered to exist: a monomer and a disulfide-bonded homodimer [8, 9]. Oxidative stress is an imbalance between the production and elimination of reactive oxygen species (ROS) in the body. Many biological components, primarily lipids and polyunsaturated fatty acids, are targeted by ROS [10]. Malondialdehyde (MDA), along with other aldehydes, is one of the most thoroughly researched byproducts of polyunsaturated fatty acids peroxidation [11]. The aims of the current context were to assess the level of serum MMP-9 and MDA in children with nocturnal enuresis and to look for a relation between MMP-9 and nocturnal enuresis children.

2. Subjects and methods

Patients

This cross-sectional comparison study evaluated adolescence with Nocturnal enuresis in accordance with the institutional research board's ethical standards and received clearance from the local ethical committee (Code No. MD.21.03.64). Fifty-three with nocturnal enuresis and 47 children Healthy controls. All children age 10 -18 years) referred to the Urology & Nephrology center. Mansoura university Nephrology were included in the study. For children in the control group attended outpatient clinics for standard checkups or healthy child examinations.

Sample collection:

3 ml of blood without anticoagulant was taken and centrifuged at 300xg for 10 min and stored at -20C until used for the investigation of biochemical analysis.

Measurement of MMP-9

MMP-9 was measured by ELISA Kit (Cat. No: E-EL-H6075) (enzyme-linked immunosorbent assay) from Elabscience. according to manufacture instruction. This sandwich kit is for the accurate quantitative detection of Human MMP-9.

Measurement of Malondialdehyde (MDA)

MDA level was measure in serum according to

the methods of Ohkawa et al [12], Thiobarbituric acid (TBA) and MDA react at 94 °C for 30 minutes to produce a pink, 532 nm-measurable compound that is reactive with thiobarbituric acid (TBA).

Statistical analysis

SPSS software, version 18 (SPSS Inc., PASW statistics for Windows version 18), was used to analyse the data. SPSS Inc., Chicago. Number and percentage were used to describe qualitative data. After testing for normality using the Kolmogorov-Smirnov test, quantitative data were described using the median (minimum and maximum) (interquartile range) for non-normally distributed data. The acquired results' significance was assessed at the (0.05) level. As necessary, Chi-Square was utilised to compare qualitative data between groups..

3. Results

Table 1: The age and gender of control and patients groups.

		Control group (n=47)	Cases Group (n=53)	Test of significance	P-value
Age (years) mean±SD		13.06±2.05	13.29±2.01	t=0.56	0.567
Gender	Males n (%)	20 (42.6%)	28 (52.8%)	X ² =1.05	0.305
	Female s n (%)	27 (57.4%)	25 (47.2%)		

Characteristics of adolescent nocturnal enuresis patients and healthy controls are shown in the current study. From Table 1, the study participants involved 53 patients (Cases) suffering from nocturnal enuresis and healthy controls contained 47 apparently healthy individual.

Their ages ranged from 10 to 18 years.

There were no significant differences in age and gender of patients with nocturnal enuresis in comparison to control group (p = 0.567 and 0.305, respectively).

Table 2. The level MDA and MMP-9 within studies groups

	Control group (n=47)	Cases Group (n=53)	Test of Significance	P-value
MMP-9 (pg/mL)	128.42 (45.78-203.59) (84.34-156.11)	132.37 (55.23-253.03) (95.05-192.07)	Z=0.925	P=0.355
MDA (nmol/mL)	(0.25-9.18) (2.16-5.62)	4.55 (0.69-22.51) (2.78-7.37)	Z=1.59	P=0.112

Z: Mann Whitney U test. Parameters are described as median (min-max) (interquartile range). P is significant when < 0.05 . * Statistically significant

Regarding serum mmp9 non-significant difference between cases and control groups (132.37 vs 128.42, respectively) ($P>0.05$). Using the ELISA test shown in (Table 2). Also, we found non-significant difference was detected between cases and control groups in MDA (4.55 vs 3.43 respectively) ($P>0.05$).

4. Discussion

In this study, as nocturnal enuresis (NE) was examined to demonstrate the presence and activity of MMP-9 and MDA. Enuresis, often known as nocturnal enuresis (NE), is a typical childhood issue. Enuresis frequently causes parents and children great distress, and it frequently has a negative impact on family life. Along with domestic violence, other issues like low self-esteem, social exclusion, poor academic achievement, and psychological impairment have been mentioned [13]. NE is divided into primary, secondary, monosymptomatic (MNE), and nonmonosymptomatic (NMNE) types. Lower urinary tract (LUT) dysfunction symptoms are absent in children with MNE, and their voiding volumes are often within the normal range [14]. Matrix metalloproteinases (MMPs), an important class of zinc-dependent proteolytic enzymes, have the ability to break down extracellular matrix components and other barriers. MMP2 and MMP9, in particular, have been found to cleave collagen IV in the basement membrane to facilitate cell invasion in cancer cells [15]. In our study, the serum MMP-9 level did not differ in the case group compared with the control group. Recently, (Kudelski, et al., 2023) found significantly higher levels of the content and specific activity of MMP-9 were increased in urinary bladder cancer.[16]

Furthermore, based on the findings from the current study, the serum MDA level did not differ in the case group compared with the control group. MDA is recognized as oxidative stress marker. MDA, a lipid peroxide product, reflects the severity of damage caused by free radicals [17]. Miao-Shang Su et al., found that MDA content in serum is significantly high in the rat model of chronic intermittent hypoxia (CIH)-induced enuresis[18].

Conclusion and recommendations

Nocturnal enuresis were found non difference between studied groups in MMP-9 and MDA in cases group compared to control group. More studies are recommended to understanding the development of the disease and its prevention.

5. References

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