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Review

Biochemicals and DNA Degradation Identifier Markers of Postmortem Time Interval in Different Causes of Death

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Abstract

Postmortem time interval has significance in forensic medicine even in natural deaths due to have importance in legal matters, such as crime, inheritance, civil, disasters and insurance issues. Till now there is no definitive marker identify postmortem time interval, even there is major research articles published in this topic. there many factors affecting PMI such as sex, age, environmental condition, status at onset of death and causes of death. groups of biochemicals in blood, vitreous humor, bone marrow and tissues can be helpful for determination of PMI at each time point elapsed after death. Also, loss of DNA integrity and quailty have potential role of PMI determination except some cases which delay or replace the putrefaction.

Key words: *Postmortem time interval, Trace mineral, Biochemicals, DNA degradation.*

BIOCHEMISTRY OF POSTMORTEM TIME INTERVAL

Trace Mineral as Biochemical Markers

Causes of death have a role in PMI determination. for example, they sudy the estimation of potassium, sodium concentrations and osmolarity of VH, CSF and heart blood on freshwater drowning and other causes of death. They found that K^+, Na^+ levels and osmolarity lower in case of drowning compared to other cases.[1] Also, there was no significant correlation between PMI and increase in serum Ca and Mg. Both Ca and Mg concentrations in peripheral blood and heart had a remarkable increase in saltwater drowning compared to other causes of death. Additionally, there was a significant rise in the Ca level in freshwater drowning and burn and in Mg level in fatal methamphetamine (MA) intoxication and asphyxia.[2] These markers may be helpful for diagnosis and differentiation of fresh- and saltwater drownings and may be also useful for determination of the causes of death associated with skeletal muscle damage, including burns and MA intoxication. While the changes in concentration of sodium in vitreous humor could be useful for investigation of immersion associated deaths. Also, these changes might be helpful to descrimination between fresh- and saltwater drowning.[3] Notably, the postmortem Sodium and Chloride levels changes of VH were useful for determination of saltwater drowning and immersion cases but Magnesium was more specific to immersion.[4]

The changes in levels of certain chemicals in vitreous humor, blood and CSF for different intervals. Results were as following postmortem vitreous humor potassium levels elevated along with PMI and raised temperature, CSF potassium and phosphorus levels showed marked increase, chloride levels lowered and creatinine and calcium levels slightly increased. Blood potassium, creatinine and phosphorus concentrations increased; sodium and chloride concentrations were decreased.[5] Moreover, blood carbon dioxide concentrations decreased at 6-hours after death to a quarter of concentrations at antemortem. Notably, a linear time dependent elevation in the concentration of vitreous humour potassium level with post mortem time interval and this elevation was not affected by ambient temperature, humidity, sex and age.[6] In consistent, the vitreous potassium concentration showed linear fashion of increase along with post-mortem interval. So, PMI can be accurately calculated through applying certain formula and PMI was not sex, age or ambient temperature dependent.[7]

The analysis of vitreous humor there was a significant positive correlation between PMI and potassium level (r=0.841, p=0.000) and a negative correlation between PMI and sodium (r=0.137, p=0.048) and glucose (r=0.241, p=0.000) while there was no correlation detected between PMI and calcium. (r=0.055, p=0.429) and chloride (r=0.075, p=0.11).[8] The increase in vitreous humor potassium after death followed a non-linear curve and that age and ambient temperature affect that increase by 16% and 5%, respectively, also a high alcohol level and a long duration of agony at the time of death affect potassium level change by less than 1%. So, they created two equations, one for estimation of potassium level alone and a second for potassium level correlated to age

and ambient temperature.[9] Also, the measured parameters in CSF of White New Zealand rabbits were important as sodium and potassium had an significant role in estimation of PMI at different time periods in traumatized and physical causes death.[10] Interestingly, Cordeiro et al[11] develop a free software program which calculates the PMI from the model based on detection of constituents available in vitreous humor.

Enzymology and Metabolic Product as Postmortem Time Interval Marker

In New Zealand White rabbits that urea nitrogen concentration in serum and vitreous humor showed a linearly correlation postmortem intervals while gamma-glutamyl transferase concentrations showed no significant differences in serum and vitreous humor during PMI of the study(4 to 8-hours).[12] Also, the stabilization of uric acid (UA), urea nitrogen (UN) and creatinine (Cr) levels in the pericardial fluid within 48-hours postmortem and their significant role in investigation of the pathophysiology of death. The three biochemical markers showed remarkable increase in death cases associated with azotemia such as hypothermia, hyperthermia and delayed traumatic death while in drowning they showed decreased levels.[13] Also, there was none of the biochemical markers except for triglyceride showed significant changes until three days postmortem changes while he studied the following parameters as HbA1c, fructosamine, blood nitrogen urea (BUN), creatinine, total protein, total bilirubin, c-glutamyl transpeptidase (c-GTP), triglyceride, total cholesterol, C-reactive protein (CRP) and pseudo choline esterase (pChE).[14] Inconsistent with upper report, conducted an analytic study on activity of certain pericardial fluid enzymes after death such as Gammaglutamyl Transferase (GGT), Amylase , Lactate Dehydrogenase (LDH) and Creatine Kinase (CK), They found that there was a significant correlation between these enzymes' activities and PMI especially CK which was more significant.[15]

Additionally, acid phosphatase and aminotransferases (AST & ALT) coorelated in a time dependent increase along with PMI and this increase was found to be more linear in burn cases.[16] Notably, the specific enzymes could be used to accurately determine PM as lactate dehydrogenase (LDH), creatine kinase (CK), alcohol dehydrogenase (ADH), and aspartate aminotransferase (AST) in SD rat either treated with ethanol or not.[17] Also, two mathematical models of predictive values were become important replacement tools of traditional methods to achieve a more accurate PMI estimation.[18] Through noticing a significant linear correlation between aspartate transaminase (AST), urea, transferrin, immunoglobulin M (IgM), uric acid, creatine kinase (CK), total and direct bilirubin, calcium and iron with the time of blood putrefaction. Tumor necrosis factor-a and serum-fas were increased in dependent manner until last time point after induction of natural death but creatinine, BUN, AlT, and AST had no change except little increase in 30-hours after induction of death in rats.[19]

The changes in serum catecholamine levels related to cause of death an reflect amount of stress response during death. Serum adrenaline and noradrenaline showed a significant rise in injury and asphyxiation cases and increased adrenaline only in fatal methamphetamine (MA) and other poisoning cases, while both levels were decreased in fatal hypothermia. Drowning and burns showed intermediate adrenaline and noradrenaline concentrations. The dopamine (DA) level was raised in cases of injury, MA fatality, hyperthermia and other poisoning. They also concluded that the main cause of raised serum catechol amines was injury of adrenal glands and abdominal viscera as in case of drowning, burns, hyperthermia, MA fatality, another poisoning.[20] Additionally, the urinary Adrenaline and noradrenaline levels were increased in blunt head injury, hypothermia, hyperthermia and methamphetamine poisoning, but were decreased in drowning, mechanical asphyxia, burns and sedative-hypnotic intoxication. DA increased in case of injury, drowning, burns, methamphetamine and poisoning, but it decreased in sedative-hypnotic intoxication and mechanical asphyxia. Urinary catecholamines are good indicator for different cause of death.[21]

Biochemical parameters could be varied and dependent cause of death and type of violent asphyxia as TP and Alb levels in bilateral cardiac blood were higher in hanging than strangulation.[22] Certain metabolites (lactic acid, uric acid, ammonia, hypoxanthine, NADH and formic acid) and blood pH that may be useful for PMI determination. These metabolites and blood pH showed a time dependent elevation during period of the study (96-hours).[23] Also, the protein profile of organs as kidney, brain, lung, heart, liver and pancreas analyzed by (SDS-PAGE), proved to be a significant method for determination of PMI even for a long period up to 10-days.[24]

Interestingly, at early time of 6-hours, there was a reduce on Na^+/K^+-ATPase and GST activities in the brain and liver tissues, respectively and elevate on renal GST activity. At the time point of 24-hours, an increase on the cerebral AChE and renal GST levels were observed, while the cerebral Na^+/K^+-ATPase activity was decreased. cerebral Na^+/K^+-ATPase and renal GST activities remained in reverse at 48-hours. after death, In addition, no change was observed on the GST level in the skeletal muscle and brain.[25]

DNA Degradation as Determinant Factor of PMI

DNA degradation and concentration play important role in post mortem time interval except in cases replaced putrefaction. The quantitative analysis of DNA degeneration is an effective tool for PMI investigation. By using Image analysis technique (IAT) they estimated DNA degradation in cell nucleus of brain astrocytes and spleen lymphocytes within (5 to 36-hours.) through measuring three indices including integral optical density (IOD), average optical density (AOD) and average gray (AG). They found that IOD and AOD decreased and AG increased along with PMI progress within (5-36-hours.).[26] Additionally, The changes in some indices of retinal rat cells indicated that DNA degeneration as following Integral absorbance (IA) and Average absorbance (AA) showed gradual decrease while Index of density showed elevation along with progress of time after death.[27] Notably, there is linear relationship between the degradation rate of nuclear DNA and postmortem time interval (PMI) was found in viscera like liver. While other organs like brain showed slower degradation rate of nuclear DNA. So, it is considered as a valuable organ for studying DNA in longer detection PMI.[28] Similarly, a study for detection of relationship between PMI and DNA degenerations at different intervals (3, 6, 9, 12, 24-hours) post-mortem using single cell gel electrophoresis, they noticed that cells began to change in shape and became comet-like that gradually increased in frequency and percentage that give rise to DNA degeneration increased along with increased PMI.[29]

DNA degradation was a time dependent process in evaluation tools used in PMI after (0, 24, 48-hours) in rat sacrificed by cervical dislocation. DNA from brain considered as important when compared to liver and kidney DNA in detection of post mortem time interval due to brain had slower postmortem changes. RAPD-PCR and agarose electrophoresis were used to detect the quality of DNA in different times after induced death[30] also, the percentage of DNA fragmentation increased in relation to increased oxidants level in brain and femoral muscle tissues from (0 to 96-hours) in detection of PMI in both drowning model of death and death by cervical dislocation in albino rat.[31] The quantitative

analysis of changes in DNA content of SD rat's liver, brain, kidneys and skeletal muscle at PMI (0 to 6-weeks). They stored organs at 200C and 40C then amplified DNA content measured by real-time PCR for each organ. They noticed that DNA quantity in brain showed linear decrease at 200C for 6-weeks interval, while at 40C DNA amplified quantity in liver showed slow decrease along with post-mortem time progress.[32]

FUTURE HIGHLIGHTS

The research in postmortem time interval is still controversial and need to use advanced technology to enrich this branch of science. Also, the researcher should put in consideration different causes of death in human or animal affect postmortem time interval.

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CONFLICT OF INTERESTS

The author declares no conflict of interests.

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