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Interpretation of postmortem vitreous concentrations of sodium and chloride

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ABSTRACT

Vitreous fluid can be used to analyze sodium and chloride levels in deceased persons, but it remains unclear to what extent such results can be used to diagnose antemortem sodium or chloride imbalances. In this study we present vitreous sodium and chloride levels from more than 3000 cases. We show that vitreous sodium and chloride levels both decrease with approximately 2.2 mmol/L per day after death. Since potassium is a well-established marker for postmortem interval (PMI) and easily can be analyzed along with sodium and chloride, we have correlated sodium and chloride levels with the potassium levels and present postmortem reference ranges relative the potassium levels. We found that virtually all cases outside the reference range show signs of antemortem hypo- or hypernatremia. Vitreous sodium or chloride levels can be the only means to diagnose cases of water or salt intoxication, beer potomania or dehydration. We further show that postmortem vitreous sodium and chloride strongly correlate and in practice can be used interchangeably if analysis of one of the ions fails.

It has been suggested that vitreous sodium and chloride levels can be used to diagnose drowning or to distinguish saltwater from freshwater drowning. Our results show that in cases of freshwater drowning, vitreous sodium levels are decreased, but that this mainly is an effect of postmortem diffusion between the eye and surrounding water rather than due to the drowning process, since the decrease in sodium levels correlates with immersion time.

1. Introduction

The postmortem diagnosis of various electrolyte imbalances is often difficult to make due to the degradation of the many cells in the blood, which makes blood or serum unsuitable for such analyses. Other body fluids that can be used for postmortem chemistry are vitreous, cerebrospinal, pericardial and synovial fluid. Among these, vitreous fluid has become the matrix of choice in forensic pathology, not only because it is much easier to obtain, but also because of its isolated position, which makes it less affected by postmortem contamination and putrefaction [1–3]. Further, vitreous fluid is almost devoid of cells, and the changes occurring after death are almost exclusively an effect of postmortem exchange of ions and other endogenous compounds between the vitreous and the surrounding cells. Hence, a large number of postmortem biochemistry studies have been conducted on vitreous fluid, aiming to provide keys to various diagnoses.

In this communication we focus on the diagnosis of deranged sodium and chloride levels. These can arise from a variety of illnesses, such as kidney failure, liver failure, cancer or diarrhea. In a forensic setting cases may, for example, concern:

- *dehydration* – may be very important to diagnose properly, especially in cases of neglect of children or the elderly [1,4];
- *salt intoxication* – mostly seen in children who have been force-fed salt as a punishment or due to a Munchhausen by proxy syndrome [4,5];
- *water intoxication* – a condition called psychogenic polydypsia, where psychiatric patients compulsively drink large amounts of water [6]. This can lead to brain swelling, seizures and death. Water intoxications can also occur during MDMA (3,4-methylenedioxy-methamphetamine, ecstasy) use [7];
- *beer potomania* – a condition similar to water intoxication. Large ingestion of beer, together with poor food intake, can lead to severe hyponatremia [8];
- *drowning* – hypothetically, aspiration of water during drowning leads to hyponatremia in freshwater and to hypernatremia in saltwater. Some authors have proposed that vitreous sodium/chloride levels can be used to distinguish saltwater from

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Table 1
Postmortem changes in vitreous sodium and chloride according to different authors.

Author (year)	Sodium	Chloride
Coe (1969) [22]	↓	↓
Blumenfeld (1979) [23]	→	→
Balasooriya (1984) [17]	↓	
Farmer (1985) [24]	↓	
Madea (2001) [25]	→	→
Tao (2006) [26]	↓	↓
Jashnani (2010) [20]	→	→
Tumram (2011) [21]	→	↓
Chandrakanth (2013) [27]	↓	↓
Mitchell (2013) [18]	↓	↓
Siddamsetty (2014) [19]	↓	→

freshwater drownings [9] or drownings from non-drownings [10].

Sodium is the major cation and chloride the major anion in the extracellular fluid, with normal levels being 135–145 mmol/L and 95–110 mmol/L, respectively. Sodium is the major osmotically active ion, so the serum sodium concentration normally reflects the osmolarity of the extracellular fluid and total body sodium content determines the volume of the extracellular fluid compartment. Water balance and plasma osmolarity, and thereby serum sodium levels, are tightly regulated by the kidneys, which continuously make adjustments to the concentration of urine in order to maintain constant plasma osmolarity. Extreme sodium and chloride imbalances can cause the cells in the body to swell or shrink and can be fatal [11].

There are no reliable published data on human vitreous electrolyte levels in vivo. Studies on various animals, however, have shown that vitreous sodium levels are ~95% of those in blood and vitreous chloride levels are ~110% of those in blood [12–15].

The postmortem changes in vitreous sodium and chloride levels have been studied extensively. Table 1 summarizes findings by different authors. There seems to be no real consensus about the postmortem changes of these electrolytes, although it should be mentioned that the postmortem changes that were found by some authors were marginal.

In an article from 2005 on the postmortem diagnosis of hypertonic dehydration by Madea and Lachenmeier [16] it is stated that there are several conceptual problems surrounding postmortem vitreous sodium values that still have to be resolved, for example the distribution of postmortem vitreous values in comparison to serum values in vivo and the postmortem changes.

The aims of this study were:

- To evaluate the postmortem changes of vitreous sodium and chloride.
- To investigate whether postmortem vitreous sodium levels reflect antemortem serum sodium levels and thus can be used to identify antemortem imbalances.
- To correlate sodium and chloride levels to specific causes of death.
- To establish postmortem vitreous reference concentrations of sodium and chloride.

2. Materials and methods

2.1. Study design

Between January 2003 and June 2006, vitreous fluid samples were consistently collected from all deceased subjects admitted to the Department of Forensic Medicine (Stockholm, Sweden) as soon as possible following the arrival of the bodies at the morgue ($n = 3065$). Fourteen cases were excluded due to technical analytical problems; otherwise, no cases were excluded. In order to study the changes of sodium and chloride concentrations with postmortem time, 462 cases with a known postmortem interval were selected from this period, and 62 cases from 2012 (altogether $n = 524$). When possible changes in sodium and chloride concentrations due to different medical conditions were studied, the concentrations were related either to the true postmortem interval (PMI), or to the potassium concentration as a proxy for the PMI. The latter approach provided a much larger material for comparison.

For all cases, information was extracted from the Swedish national forensic medicine database [17] and linked to the results obtained by analysis of vitreous fluid with the blood gas instrument before being anonymized. The original forensic pathology case files were perused to select cases with a certified time of death, to search for antemortem analytical results whenever copies of medical records were available and to more closely study the circumstances surrounding death and the autopsy findings.

Approximately 0.2 mL vitreous fluid was aspirated from the center of each eye using a 1 mL syringe equipped with an 18-gauge needle. The samples from each decedent were collected in the same syringe and were not pre-treated, and hence not subjected to dilution, centrifugation, or sonication. The samples were instead directly injected into an ABL 625 blood gas instrument (ABL 625, Radiometer Copenhagen, Brønshøj, Denmark). Samples that were macroscopically opaque or dirty were also directly analyzed. However, if there was a massive bleeding in the eye, no analysis of vitreous potassium analysis was performed. In addition, samples from severely decomposed bodies and infants were not consistently included, since toxicological analyses were prioritized for several of these cases if the vitreous fluid volume was very small.

2.2. Analytical principles

All analyses were made with a blood gas instrument (ABL 625, Radiometer Copenhagen, Brønshøj, Denmark). With this instrument it is possible to determine the levels of electrolytes, pH, PCO_2, PO_2, glucose, lactate and Hb. For the determination of the concentrations of the electrolytes, a voltmeter is used for measuring the difference in potential generated across an ion-specific membrane between the sample and a reference solution for the specific analyte.

2.3. Ethical aspects

All analyses were performed as a part of the forensic medicine investigation and were reported to the responsible forensic pathologist. Therefore, ethical permission was not required for the sampling and analyses conducted according to Swedish regulations. However, ethical approval was obtained for the formation of a database for these data, and for the perusal of forensic medicine files, including police reports and medical records (Regional Ethical Review Board, Stockholm 2008/231-31/3).

2.4. Statistical methods

Correlation between variables was assessed by linear regression, and differences between groups were assessed with the nonparametric Kruskal–Wallis analysis of variance (Statistica v10, StatSoft Inc., Tulsa, OK, Excel v14.5.5, Microsoft and StatPlus v5, AnalystSoft Inc.).

3. Results

In Figs. 1 and 2, postmortem vitreous sodium and chloride concentrations are plotted against potassium concentrations. Since