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Review

The role of postictal laboratory blood analyses in the diagnosis and prognosis of seizures

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ABSTRACT

Background: Epileptic seizures (ES) lead to alterations in the blood laboratory values and reflect changes in different organ systems. Here, we review the diagnostic and prognostic value of various blood laboratory values within the context of epilepsy.
Methods: Narrative review and literature search on PubMed using the term, "seizure" and various laboratory values.
Results: Laboratory markers can help clinicians determine whether an unwitnessed event was more likely to be epileptic or non-epileptic. Prolactin testing helps differentiate ES from psychogenic non-epileptic seizures (PNES) in adults and adolescents, and is associated with high specificity and moderate sensitivity. Elevations in the creatine kinase (CK) levels are common after generalized tonic-clonic seizures (GTCS) and display high specificity and moderate sensitivity. Metabolic markers such as ammonia and lactate may have diagnostic potential for postictal blood tests.
Analyzing blood postictally is important for identifying the cause of the symptomatic seizures due to endocrine, metabolic, toxic or infectious etiologies.
Finally, laboratory analyses are used for identifying patients who are at risk for developing rare, threatening complications such as rhabdomyolysis, acute renal failure (ARF) or cardiomyopathy.
Conclusions: Presently, no postictal laboratory values can definitively prove or rule out the diagnosis of an epileptic seizure. For seizures with unknown causes, simple blood tests can be a valuable aid for quickly defining the etiology, particularly with certain metabolic and toxic encephalopathies. For this reason, CK, electrolytes, creatinine, liver and renal function tests should be measured on at least one occasion. Further research is needed in order to identify new biomarkers that improve the diagnosis and prognosis of seizures and seizure-related complications.

1. Introduction

The physiologic consequences of an epileptic seizure depend on the type, length and intensity of the seizure, as well as the patient's preexisting condition.

Seizures lead to distinctive metabolic changes. Maximal neuronal excitation incites the neuroendocrine system to secrete hormones such as catecholamines and prolactin. Whole body muscle contractions and the release of catecholamines increase cerebral, muscular and cardiac oxygen demands, while impaired breathing impedes compensatory mechanisms in order to satisfy this demand. Strained tissues release metabolites such as lactate, ammonia and urea, while irritated skeletal muscles leak creatine kinase and myoglobin. Afterwards, an inflammatory reaction with cytokine release and leukocytosis occurs.

The metabolic changes listed above are most pronounced in generalized tonic clonic seizures (GTCS) and status epilepticus (SE), but even partial seizures, especially those that are accompanied by

Abbreviations: ACS, acute coronary syndrome; ADH, antidiuretic hormone; ARF, acute renal failure; AVP, arginine vasopressin; BNP, brain natriuretic peptide; CAD, coronary artery disease; CK, creatine kinase; CPS, complex partial seizures; CSF, cerebrospinal fluid; cTNI, cardiac troponin I; cTNT, cardiac troponin T; ct-proAVP, C-terminal pro arginine vasopressin; ECG, electrocardiogram; EEG, electroencephalogram; ES, epileptic seizures; ER, emergency room; FC, febrile convulsions; GH, growth hormone (somatropine); GTCS, generalized tonic clonic seizure; ICU, intensive care unit; LH, luteinizing hormone; LOC, loss of consciousness; FSH, follicle stimulating hormone; NSE, neuron specific enolase; NT-pro-BNP, N-terminal pro brain natriuretic peptide; PNES, psychogenic non-epileptic seizures; PRL, prolactin; SE, status epilepticus; SPS, simple partial seizures; SUDEP, sudden unexpected death in epilepsy; TIA, transient ischemic attack; TSE, thyroid stimulating hormone; VPA, valproic acid; V-EEG, video-EEG.

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autonomic symptoms such as periictal tachycardia, conduction block, asystole or respiratory disturbances, can lead to physiological and metabolic changes that can be analyzed with laboratory testing [1].

Our narrative review on the value of postictal blood testing is based on the following three questions:

1.) Which blood tests aid in the differential diagnosis of epileptic versus non epileptic seizures?
2.) Which blood tests can help establish the etiology? A postictal blood test will not only demonstrate the consequences of seizures, but also the preexisting alterations that may be the actual cause of the seizures (such as electrolyte disorders and metabolic encephalopathies).
3.) Which blood tests help predict potential seizure complications? While most seizures are benign, some can be complicated by rhabdomyolysis, acute renal failure and cardiomyopathies. These can be detected early on with

Table 1
Overview of studies analyzing PRL as an aid in differentiating ES from PNES after Chen and colleagues, 2005. Prolactin elevations occur in ~60% of GTCS, ~46.1% of CPS and ~6.7% of PNES.

Author, Year	Groups	Age	Setting	Time	Elevated PRL	Comments
Wilert, 2004 [19]	44 patients: 32 ES 12 PNES	18–62	V-EEG, prospective	10, 20, 30 min, 1, 6, 12, 24 h	M > 16.5 ng/ml, F > 23 ng/ml 20 min: ES 28/32 (87.5%) PNES 4/12 (33%)	Sensitivity 87.5% Specificity 66.7%
Shah, 2001 [20]	89 patients with multiple events: 36 GTCS 56 CPS 27 SPS 55 PNES	Not provided	V-EEG, prospective	Immediately after event	2x baseline level GTCS 17/36 (47.2) CPS 19/56 (33.9%) SPS 3/27 (11.1%) PNES 1/55 (1.8%)	GTCS sensitivity 47.2% CPS sensitivity 33.9% SPS 11.1% Specificity 98.2%
Alving, 1998 [21]	58 patients: 38 ES patients 20 PNES patients 4 SPS 20 CPS 16 GTCS 20 PNES	13–68	Video- or mobile EEG monitoring, prospective	15 min and 2 h after event	2x baseline level: All ES: 69% CPS 61% GTCS: 93% PNES 20.4% exact numbers not provided	All ES sensitivity 69% CPS sensitivity 61% GTCS sensitivity 93% specificity 74%
Ehsan, 1996 [31]	50 patients: 13 GTCS 17CPS 6 SPS 14 PNES	6–61	V-EEG, prospective	15 min and 1 h after event	2x baseline level: GTCS 10/13 (76.9%) CPS 15/17 (88.2%) SPS 0/6 (0%) PNES 2/14 (14.3%)	CPS sensitivity 88.2% GTCS sensitivity 76.9% SPS sensitivity 0% Specificity 85.7%
Fisher, 1991 [22]	20 patients: 9 GTCS 7CPS 4 PNES	>18	V-EEG, prospective	10–20 min after event	>36 ng/ml GTCS 5/9 (55.6%) CPS 1/7(14.3%) PNES 0/4 (0%)	GTCS sensitivity 55.6% CPS sensitivity 14,3% Specificity 100%
Rao, 1989 [2]	11 patients: 2 GTCS 4 CPS 5 PNES	13–47	V-EEG, prospective	Immediately, every 15 min for 2 h	2x baseline level GTCS 2/2 (100%) CPS 3/4 (75%) PNES 0/5 (0%)	GTCS sensitivity 100% CPS sensitivity 75% Specificity 100%
Wroe, 1989 [23]	33 patients: 8 GTCS 11 CPS 4 Absence 10 PNES	15–73	V-EEG, prospective	10 min after event	>45 ng/ml GTCS 6/8 (65.6%) CPS 5/11 (Absence 0/4 (0%) PNES 0/10 (0%)	GTCS sensitivity 65.6% CPS sensitivity 45.5% Absence sensitivity 0% Specificity 100%
Laxer, 1985 [24]	70 patients, multiple events 64 ES 21 PNES	9–54	V-EEG, prospective	Within 20 min after event and at 24 h	25 ng/ml ES 40/61 (65.6%) PNES 1/18 (5.6%)	Sensitivity 65.6% Specificity 94.4%
Pritchard, 1985 [25]	12 patients: 1 GTCS 5 CPS 6 PNES	Not provided	V-EEG, prospective	15 min after event	2x baseline level GTCS 1/1 (100%) CPS 5/5 (100%) PNES 0/6 (0%)	GTCS sensitivity 100% CPS sensitivity 100% Specificity 100%
Oxley, 1981 [18]	18 patients, multiple events 6 GTCS 4 CPS 10 PNES	Not provided	Mobile EEG, prospective	Within 20 min after event	>36 ng/ml GTCS 4/6 (75%) CPS 0/4 (0%) PNES 1/10 (10%)	GTCS sensitivity 75% CPS sensitivity 0% Specificity 90%
Chen, 2005 [4]	Pooled analysis of the studies mentioned above	GTCS: sensitivity 60% (48.9–71.1). specificity 95.9% (91.4–100) CPS: sensitivity 46.1% (36.5–55.7). specificity 96.3 (92.7–99.9) All ES: sensitivity 52.6% (47–58.2). specificity 92.8 (89.9–95.7)				