1   **Diagnosing dehydration? Blend evidence with clinical observations**

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24   **Running Head**

25   Diagnostic Considerations for Dehydration

26

ABSTRACT

Purpose of Review

The purpose of the review is to provide recommendations to improve clinical decision making based on the strengths and weaknesses of commonly-used hydration biomarkers and clinical assessment methods.

Recent findings

There is widespread consensus regarding treatment, but not the diagnosis of dehydration. Even though it is generally accepted that a proper clinical diagnosis of dehydration can only be made biochemically rather than relying upon clinical signs and symptoms, no gold standard biochemical hydration index exists. Other than clinical biomarkers in blood (i.e. osmolality, BUN/creatinine) and in urine (i.e. osmolality, specific gravity), blood pressure assessment and clinical symptoms in the eye (i.e. tear production, palpitating pressure) and the mouth (i.e. thirst, mucous wetness) can provide important information for diagnosing dehydration.

Summary

It is recommended that clinical observations based on a combination of history, physical examination, laboratory values, and clinician experience remain the best approach to the diagnosis of dehydration.

Keywords

hydration assessment, hypovolemia, fluid balance, body water, hydration status

47 **INTRODUCTION**

48 Adults and children continuously lose and replace body water, and often develop mild, but not

49 clinically significant dehydration several times each week. Although very mild dehydration of 1.5

50 – 2 % body mass loss alters mood and results in reduced cognitive (1, 2) and physical (3)

51 performance, it is easily corrected. When left chronically untreated, moderate-to-severe

52 dehydration increases the risk of urinary tract infection, chronic kidney disease (4-6), and also

53 increases medical costs, morbidity, and mortality (7). Unfortunately, despite numerous

54 investigations (8), the methods of dehydration assessment have not been refined to the point

55 that a single reference standard has been identified for clinical decision making (9); this

56 magnifies the difficulty of diagnosing dehydration in clinical practice (9-12). This article provides

57 recommendations to improve clinical decision making based on the strengths and weaknesses

58 of commonly-used hydration biomarkers and clinical assessment methods.

59

60 **Scientific evidence that informs clinical observations**

61 We approached this problem from three perspectives: (a) rating the scientific and clinical value

62 of hydration assessment techniques; (b) rating the time, monetary cost, and technical expertise

63 required; and (c) incorporating the conclusions of previously published review papers. Table 1

64 provides a synthesis of the findings of previous publications (9, 13-16) and consensus of the

65 present authors.

66 [Table 1]

67 There is widespread consensus regarding treatment, but not the diagnosis of dehydration.

68 Although it is generally accepted that a proper clinical diagnosis of dehydration can only be

69 made biochemically (e.g. using clinical laboratory tests), rather than relying upon clinical signs

70 and symptoms (Table 1) (16), no gold standard biochemical hydration index exists (13, 16).

71 The techniques presented in Table 1 include signs and symptoms that are frequently used in

72   clinical practice for screening purposes because of their relative simplicity, speed of

73   measurement and low cost. Unfortunately, the teaching and choice of signs and symptoms are

74   largely based on clinical experience and medical tradition (11, 16); very often, the underpinning

75   scientific evidence supporting their use is weak (e.g., lack of comparison to a recognized

76   criterion or reference standard). The holy grail of identifying a single gold standard hydration

77   index is unrealistic given that the clinician evaluates different types of dehydration (e.g.

78   hypertonic and isotonic), different severities of dehydration, and often observes a patient only

79   once (i.e., static assessment in an emergency department), as opposed to monitoring hydration

80   relative to a euhydrated baseline (i.e., dynamic assessment in a nursing facility). Further, the

81   clinician accounts for the potentially confounding effects of illness and medications, and

82   considers the desired precision, accuracy, cost, analytical time and expertise required to

83   perform the measurement (Table 1).

84

85   Blood osmolality has been proposed as a suitable index of dehydration (typically defined as >

86   300 mOsm·kg^{-1}) (9, 12); however, this is not universally accepted (13, 17). Evidence supporting

87   blood osmolality as a hydration index typically comes from studies that incorporate a sweat-loss

88   model of hypertonic hypovolemia in young, fit, and healthy individuals. As such, blood osmolality

89   is unsuitable to detect isotonic hypovolemia that often results from illness and medications (e.g.,

90   diuretics) in a clinical setting. This situation is compounded by a lack of standardization in blood

91   osmolality measurements (calculated values versus direct measurements via osmometer, Table

92   1) and other clinical laboratory indices of hydration.

93

94   Guidelines for the treatment of dehydration are widely accepted, as published by the U.S.

95   Centers for Disease Control and Prevention, the World Health Organization, the American

96   Academy of Pediatrics, and the National Institute for Health and Clinical Excellence of the

97   United Kingdom. Guidelines for the diagnosis of dehydration are not universally accepted.

98

99   **The decision algorithm**

100   From the clinical perspective, volume depletion (loss of sodium from the extracellular space)

101   and dehydration (loss of water from the intracellular space) must be distinguished because this

102   influences the type and rate of fluid and electrolyte replacement. At this time, the evaluation for

103   both remains largely a clinically based process incorporating the patient history, physical

104   examination, and available laboratory values. The history and presenting circumstances often

105   drive the decision algorithm. Confounding factors influence the decision to treat for dehydration,

106   including intravascular volume depletion in the face of obvious total body water increase with

107   peripheral edema on physical exam.

108   [Figure 1]

109   Clinical observations such as skin turgor, mucous membrane moisture, sunken eyes, and tear

110   production can be helpful in children when multiple findings are present, but are not as reliable

111   in the elderly (16). Physical examination measurements such as orthostatic blood pressure and

112   heart rate responses support the clinical observation of dehydration. However, orthostatic

113   changes can be difficult to obtain in a compromised patient and may reflect dilated lower

114   extremity vasculature in an athlete post competition. Body weight can vary from day to day and

115   is useful in the acute clinical setting when there is a reasonable baseline weight to compare to

116   the current weight; however, variations in scales make this assessment less reliable. The

117   admission body weight measurement provides a useful baseline to assess body fluid changes,

118   especially when measured within a 24-h period on the same scale.

119

120 Clinical laboratory values are helpful in the context of the history and physical exam.

121 BUN/creatinine ratio, hematocrit/hemoglobin ratio, serum sodium concentration, serum

122 osmolality, and urine specific gravity are commonly measured in clinics, emergency

123 departments and on the wards, but have not been validated as a reference standard. In

124 particular, urine specific gravity reportedly is unreliable in diagnosing dehydration in children

125 with gastroenteritis (18). Medications, especially from the diuretic classes, can confuse the

126 biochemical picture by varying the renal clearance of water and electrolytes. Invasive

127 procedures with central intravascular lines help establish the volume status and fluid balance of

128 critically ill patients, but are not used in non-critical dehydration patients. Chronic kidney

129 disease, heart failure, and other maladies that affect renal blood flow also confound the clinical

130 picture and complicate diagnostic efforts. Recent evidence further complicates the assessment

131 of hydration status, in that different hydration indices may validly identify dehydration in one

132 circumstance but not another (19).

133

134 **CONCLUSION**

135 Clearly, a pressing need exists for well-controlled studies of clinically relevant dehydration

136 models (i.e., both hypertonic and isotonic hypovolemia) in appropriate patient populations (i.e.,

137 other than athletes and military personnel) that identify hydration indices with scientific and

138 clinical validity and precision. Only then can normal and clinically significant population ranges

139 be determined. At present, clinical observations based on a combination of history, physical

140 examination, laboratory values, and clinician experience remain the best approach to the

141 diagnosis of dehydration. Figure 1 and Table 1 provide guidance to that end.

142

143 **KEY POINTS**

144 • Clinical observations based on a combination of history, physical examination, laboratory

145 values, and clinician experience is the best approach to the diagnosis of dehydration.

146 • There is widespread consensus regarding treatment, but not the diagnosis of

147 dehydration.

148 • There is a pressing need for well-controlled studies of clinically relevant dehydration

149 models in appropriate patient populations (i.e., other than athletes and soldiers) that

150 identify hydration indices with scientific and clinical validity and precision.

151

156 **Conflicts of interest**

157 **LEA** is currently a consultant for Drinking Water Research Foundation, Alexandria VA and

158 Danone Research, France; has received grants from Danone Research, France; is on the

159 speaker's bureau for Drinking Water Research Foundation, Alexandria VA and Danone

160 Research, France. **SAK** is currently a consultant for Quest Diagnostics, Secaucus, NJ and

161 Danone Research, France; has active grants with Danone Research, France; is on the

162 speaker's bureau for Danone Research, France. **NPW** has received a grant with HydraDX.

163 **WOR** None.

164

165 **REFERENCES AND RECOMMENDED READING**

166 Papers of particular interest, published within the annual period of review, have been highlighted

167 as:

168 *   of special interest

169 **   of outstanding interest

170

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229

230 **Figure 1 Legend**

231 Physical examination and laboratory measurements aid diagnosis when multiple findings exist

232

233 **Table 1 Title**

234 Comparison of research and clinical techniques to diagnose dehydration during a single

235 examination.

236

237

238   Table 1

Table 1. Comparison of Research and Clinical Techniques to Diagnose Dehydration, Using a Single Measurement.

Hydration Assessment Techniques	Patient Self-Evaluation	Cost Efficiency	Time Efficiency	Simplicity of Test	Scientific Value[c]
Signs & Symptoms					
Dry mucous membrane		●●●●●	●●●●●	●●●○○	●○○○○
Skin turgor		●●●●●	●●●●●	●●○○○	●○○○○
Nail bed refill time (sec)		●●●●●	●●●●●	●●●○○	●○○○○
Thirst sensation (thirst scale rating)	✓	●●●●●	●●●●●	●●●●●	●●●○○
Respiratory pattern		●●●●●	●●●●●	●●●●○	●○○○○
Dry axilla		●●●●●	●●●●●	●●●●●	●○○○○
Seated systolic blood pressure (mmHg)		●●●●●	●●●●○	●●●●○	●●●●○
Blood pressure change supine/upright[a] (mmHg)	✓	●●●●●	●●●●○	●●●●○	●●●●○
Heart rate change supine/upright (beats·min⁻¹)	✓	●●●●●	●●●●●	●●●●●	●●○○○
Absence of tears		●●●●●	●●●●●	●●●●●	●○○○○
Sunken eyes		●●●●●	●●●●●	●●●●●	●○○○○
Palpated intraocular pressure		●●●●●	●●●●●	●●●●●	●○○○○
Dark urine color (color chart rating)	✓	●●●●●	●●●●●	●●●●●	●●●○○
Body mass (kg)	✓	●●●●●	●●●●●	●●●●●	●○○○○
Clinical Diagnostic Laboratory Tests					
BUN/creatinine ratio		●●●○○	●●●○○	●●●○○	●●●●●
Serum sodium concentration (mEq·L⁻¹ or mmol·L⁻¹)		●●●○○	●●●○○	●●○○○	●●●○○
Blood osmolality, calculated (mOsm·kg⁻¹ or mmol·kg⁻¹)		●●●○○	●●●○○	●●○○○	●●●●○
Hematocrit/hemoglobin ratio		●●●○○	●●●○○	●●●○○	●●●○○
Mean corpuscular volume (fL)		●●●○○	●●●○○	●●●○○	●●●○○
Urine specific gravity		●●●●●	●●●●○	●●●●○	●●●●○
Research Measurements					
Isotope dilution, total body water (L)		●○○○○	●○○○○	●○○○○	●●●○○
Neutron activation analysis, fluid volumes and ionic content		●○○○○	●○○○○	●○○○○	●●●○○
Bioelectrical impedance analysis, total body water (L)		●●●●○	●●●●○	●●●●○	●●●○○
Body mass (kg)	✓	●●●●●	●●●●●	●●●●●	●○○○○
Blood osmolality, measured[b] (mOsm·kg⁻¹ or mmol·kg⁻¹)		●●●○○	●●●○○	●●●○○	●●●●○
Urine osmolality (mOsm·kg⁻¹ or mmol·kg⁻¹)		●●●●○	●●●●○	●●●●○	●●●●●
Salivary osmolality (mOsm·kg⁻¹ or mmol·kg⁻¹)		●●●●○	●●●●○	●●●●○	●●●●○
Tear osmolarity (mOsm·L⁻¹ or mmol·L⁻¹)		●●●●○	●●●●○	●●●○○	●●●○○
Intraocular pressure (mmHg)		●●●●○	●●●○○	●●●○○	●●○○○

[a] lying to sitting, sitting to standing, lying to standing
[b] measured via freezing point depression osmometry
[c] considering measurement resolution, reliability and accuracy

●●●●● = high, ●●●○○ = medium & ●○○○○ = low

239

240   Figure 1

Absence of tears
Sunken Eyes
Palpate Pressure

Dry mucous membrane
Thirst
Salivary osmolality

Change in BP
supine/standing: ≥20 mmHg
Seated systolic BP: ≤100 mmHg

Blood Osmolality: ≥300 mmol/kg
BUN/Cr: ≥20

Osmolality: ≥800 mmol/kg
USG: ≥1.025

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