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Yüksek Serum Osmolalitesi Akut Ülseratif Kolit Hastalarında Hastalık Şiddetini Tahmin Edebilir

High Serum Osmolality May Predict the Disease Severity in Patients with Acute Ulcerative Colitis

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ÖZ

Amaç: Ülseratif kolit (ÜK), kolon mukozasının kronik immün aracılı enflamasyonu ile karakterizedir. ÜK'nin ciddiyetini tanımlamak için Truelove ve Witts (TW) kriterleri kullanılmıştır. Diğer taraftan, ÜK'li yüksek riskli hastaların daha iyi tanımlanabilmesi için daha basit bir laboratuvar aracına ihtiyaç vardır. Çalışmanın amacı, özellikle acil servis uygulamalarında, hastanın semptomatik tedaviden sonra hastaneye yatırılması gerekliliğini öngörebilen ve hastalığın ciddiyetini kolayca ve hızlı bir şekilde tahmin edebilen bir biyobelirteç olarak serum osmalalitesinin yararlılığını belirlemektir.

Materyal ve Metot: Bu tek merkezli, retrospektif kohort çalışmasında ÜK'li 62 hastanın demografik özellikleri ve kan örnek sonuçları değerlendirildi ve veriler toplandı. Serum osmolalitesi ile birlikte hastaların Truelove ve Witts (TW) skorları hesaplandı. Data analizinde stata 14.0. paket programı kullanıldı. P < 0,05 istatiksel olarak anlamlı kabul edildi.

Bulgular: Çalışma sonunda, yüksek osmolaliteli hastaların daha yüksek olasılıkla şiddetli ülseratif kolite, yüksek TW skoru, sahip oldukları görülmüştür.

Sonuç: Sonuç olarak, serum osmolalitesi hastalığın ciddiyetini göstermek için yararlı bir belirleyici olarak düşünülebilir.

Anahtar Kelimeler: Akut ülseratif kolit, serum ozmolalitesi, Truelove Witt's skoru

ABSTRACT

Objective: Ulcerative colitis (UC) is characterised by chronic immun- mediated inflammation of the colonic mucosa. The Truelove and Witts (TW) criteria have been used to define the severity of the UC. Otherhand, a simplier and unified laboratory tool is needed for better definition of high risk patients with UC. The aim of the study, especially in emergency service applications, was to determine the usefulness of serum osmalality as a biomarker which can easily and rapidly predict the severity of the disease, in which the patient will be advised to be hospitalized after the symptomatic treatment.

Materials and Methods: In this single-center, retrospective cohort study, we collected data of 62 hospitalized patients with UC such as demographic characteristics and blood sample results evaluated by clinicians. Truelove and Witts (TW) scores of the patients along with serum osmolality were calculated. Stata 14.0. package program was used for data analysis. P <0.05 was considered statistically significant.

Results: According to our results, patients with hyperosmolality were more likely to have severe UC as defined by having higher scores of TW criteria at baseline.

Conclusion: As a conclusion, serum osmolality can be considered as an useful predictor to demonstrate the severity of the disease.

Keywords: Acute ulcerative colitis, serum osmolality, Truelove Witt's score

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INTRODUCTION

Ulcerative colitis (UC) is characterised by chronic immun- mediated inflammation of the colonic mucosa. One-fifth of patients with UC will experience an acute flare requiring hospitalization. This is a medical emergency and requires prompt recognition and multidisciplinary management.[1] Active disease in severe UC also causes a major health burden with increasing global incidence of the disease.

Colonoscopy is the standart procedure for diagnosing ulcerative colitis and histopathological examination of the biopsy specimens of the colonic mucosa usually shows lympocytic cryptit and distortion of the villi.[2]

The Truelove and Witts (TW) criteria have been used to define the severity of the UC since 1954.[3] and this criteria are most widely used to define active severe colitis.[4,5] TW score measures disease activity based on the mucosal ulcers and fragility in connection with some laboratory parameters and is a robust tool for clinical approach to the patient. Calculation of TW scores may help in stratifying the risk of disease activity and detailed screening and surveillance**.** The TW-based severe UC is defined as more than six blood stained stools daily, with 1 or more of the 4 additional criteria: hemoglobin level below than 10.5 g/dl, erithrocyte sedimentation rate higher than 30 mm/hour, fever higher than 37.8^{0}C, and sinus tachycardia greater than 90/min.[6]

Serum osmolality is a key element of neurohormonal activation and may influence to certain medical agents in patients with severe illnesses such as hearth failure.[7] In normal subjects, the serum osmolality is calculated from the following formula: Plasma osmolality (mOsm/kg) = 2x(Na^++K^+) + glucose/18 + urea/6 (glucose and urea are expressed as mg/dL, while K^+ and Na^+ in mmol/L). If urea nitrogen (BUN) is measured, then the BUN/2.8 should be utilized in the equation instead of urea/6 is also acceptable.[8] In normal conditions, serum osmolality are ranged from 275 to 295 mOsm/kg.[9]

Otherhand, a simplier and unified laboratory tool is needed for better definition of high risk patients with UC. However, there is no consensus for the value of serum osmolality during pre-colonoscopy period for those patients with severe UC.

MATERIALS AND METHODS

In this single-center, retrospective cohort study, we collected data from 62 patients with ulcerative colitis who were hospitalized to hospital between 1 January 2017 and 1 July 2018 and evaluated by gastroenterologists. These data were collected retrospectively from a national university training and research hospital data system and official approval was obtained for the use of this data (29.05.2020 / 85554271-929). Patients who were pregnant or younger than 17 years old or were taking steroids, mannitol, radiocontrast agents, alcohol, ethylene glycol were excluded from this analysis. In addition, patients with surrenal and thyroid diseases were also excluded from the study.

The following information was extracted: age, gender, hematologic and biochemical markers, serum levels of TSH, cortisol, Na^+, K^+ , glucose, urea, creatinine and albumin. We diagnosed acute severe colitis using the conventional Truelove and Witts criteria and serum osmolarity was calculated using the equation (2 × Na^+ + K^+) + (glucose/18) + (BUN/2.8).[8,10]

Statistical Analysis: If a P value was lower than 0.05, it was considered as statistically significant. All confidence intervals (CI) quoted are 95% CI. Multivariate logistic analysis was performed to calculate odds ratios, adjusting for sociodemographics, patient characteristics, comorbidities and code status. Analysis was performed using Stata 14.0.

RESULTS

The age (mean ±SD) of participants was 54.5±6.5 years and 30 (48%) were women. At baseline, UC duration (mean±SD) was 4.2 ±2.8 years. Two-thirds had extensive colitis and one-third had higher TW scores. The baseline characteristics of patients in the study were shown in Table 1.

According to our study results; Patients with hyperosmolality were more likely to have severe UC as defined by having higher scores of TW criteria at baseline .

Cross sectionally, higher serum osmolality was correlated with higher baseline creatinine (r=-0.1, CI=0.7 to 0.8; p<0.001), higher CRP (r=0.8; CI: 0.3 to 1.2; p=0.01), higher WBC (r=3.2; CI:6.6 to 8.5; P=0.016), greater MCV (r=8.9; CI=82 to 87; p=0.018); lower hematocrit (r=5; CI=37 to 41; p= 0.043) and lower albumin (r=0.5, CI=4.5 to 4.8; p<0.001) levels. A summary of the data can be found on Table 2.

DISCUSSION AND CONCLUSION

Serum osmolality plays a key role in extracellular and intracellular osmotic status and determined by the concentrations of Na+, K+, Cl–, glucose and urea. Hyperosmolality mostly caused by detoriation of main contributing elements of the serum osmo-

lality including serum sodium and serum glucose in critically ill patients.[11,12]

It has been also demonstrated that dehydration and hypernatraemia could cause elevated serum osmolality in patients with gastrointestinal disorders with thresholds at 300 mmoL/L. Hyperosmolarity was also linked to increased hospital and ICU mortality compared with normal osmolarity levels.[13] The normal range of serum osmolality is defined as 275-295mOsm/kg of water.[9] It has been showed that increased resting sympathetic activity and blood pressure could be related to acutely elevated plasma osmolality.[14]

In a recent publication authors reported that UC also triggers a complex cascade of metabolic responses that can cause fluid-electrolyte disturbances such as hypernatremia. Authors also showed that colonic dysfunction is an important contributor to serum osmolality, due to the critical roles of colonic mucosa for regularity of sodium and electrolyte balance.[15,16]

In vitro studies of the net transport and concomitant two-way influx rates of water and electrolytes along the human colonic epithelium showed that in case of UC the colon had diminished capacity absorption and had increased capability of secretion. Specifically, in the acute severe UC; colon absorbs less water and salt and secretes more potassium.[17]

There were several limitations of the study. First, patient bias may have been existed due to retrospective nature of the study. Second, study findings may not be generalized entire the population due to small sample size. Lastly, we did not obtain the data involving osmolal gap.

Further studies are needed to determine a causal link between serum osmolality and UC.

As a conclusion; Serum osmalality can be considered as a useful tool in demonstrating the severity of the disease in addition to clinical, hemodynamic and other laboratory tests of patients as a guide in the management of patients admitted to the hospital with ulcerative colitis attack. The serum osmalality as a laboratory marker can be useful and should be part of the global management of UC patients. But further studies are needed to determine a causal link between serum osmolality and UC because of several limitations of the study.

Ethics Committee Approval: In this single-center, retrospective cohort study, the data were collected retrospectively from a national university training and research hospital data system and official approval was obtained for the use of this data. (29.05.2020 / 85554271-929)

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept-ACD; Supervision- SV; Materials - AV, ST; Data Collection and/or Processing - AV, ST; Analysis and/ or Interpretation-ACD, AV; Writing -AV, ACD.

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Table 1. Baseline characteristics of the patients in the study (n: 62).

	Minimum	**Maximum**	**Mean±SD**
	Statistic	**Statistic**	**Statistic**
Age	19.00	78.00	54.1250±17.31445
Hemoglobin (gr/dl)	10.20	17.50	12.7031±1.77482
Anion gap (mEq/L)	12.70	19.30	15.5222±1.99987
Osmolality (mOsm/kg)	288.50	309.00	295.7438±5.42693
Chlorine (mmol/L)	97.00	107.00	101.9688±2685
Hematocrit (%)	32.60	52.70	39.4813±4.64518
Tsh (mIU/L)	0.22	5.44	1.8965±1.33913
Sodium (mmol/L)	138.00	148.00	142.0000±2.31405
Ferritine (ng/mL)	4.18	229.20	54.7973±59.45761
Crp (mg/dL)	0.03	4.93	0.8106±1.16337
Potassium (mmol/L)	3.83	5.41	4.7003±0.34951
MCV (fL/red cell)	68.80	96.90	85.0563±6.14124
ALT (IU/L)	4.00	66.00	22.4375±17.16887
Albumine (mg/dl)	3.50	5.30	4.6967±0.45749
Creatinine (mg/dl)	0.52	1.25	0.8003±0.20421
Wbc (x 10^9/L)	2.64	15.39	7.5981±2.50219
Glucose (mg/dl)	84.00	220.00	115.9063±32.33530
Plt (x 10^3/µL)	128.00	438.00	279.9688±85.34578
Urea (mg/dl)	11.00	49.00	30.2813±10.39303
AST (IU/L)	9.00	68.00	22.6250±12.32032

Table 2. Comparison of osmolality with other parameters.

ANOVA TEST		Sum of Squares	df	Mean Square	F	Sig
Age	**Between Groups**	9037.833	25	361.513	8.484	0.007
	Within Groups	255.667	6	42.611		
	Total	9293.500	31			
Hemoglobin (gr/dl)	**Between Groups**	90.665	25	3.627	3.115	0.080
	Within Groups	6.985	6	1.164		
	Total	97.650	31			
Chlorine (mmol/L)	**Between Groups**	141.302	25	5.652	1.433	0.346
	Within Groups	23.667	6	3.944		
	Total	164.969	31			
Potassium (mmol/L)	**Between Groups**	3.415	25	0.137	2.206	0.164
	Within Groups	0.372	6	0.062		
	Total	3.787	31			
Creatinine (mg/dl)	**Between Groups**	1.273	25	0.051	15.272	0.001
	Within Groups	0.020	6	0.003		
	Total	1.293	31			
Tsh (mIU/L)	**Between Groups**	53.000	25	2.120	4.908	0.028
	Within Groups	2.592	6	0.432		
	Total	55.592	31			
Sodium (mmol/L)	**Between Groups**	158.333	25	6.333	4.957	0.027
	Within Groups	7.667	6	1.278		
	Total	166.000	31			
Ferritine (ng/mL)	**Between Groups**	97937.838	23	4258.167	5.575	0.020
	Within Groups	4583.163	6	763.860		
	Total	102521.001	29			
CRP (mg/dL)	**Between Groups**	40.092	24	1.671	19.633	0.010
	Within Groups	0.511	6	0.085		
	Total	40.603	30			
ALT (IU/L)	**Between Groups**	8439.375	25	337.575	2.900	0.094
	Within Groups	698.500	6	116.417		
	Total	9137.875	31			
Albumine (mg/dl)	**Between Groups**	5.978	23	0.260	17.012	0.001
	Within Groups	0.092	6	0.015		
	Total	6.070	29			
AST (IU/L)	**Between Groups**	4310.333	25	172.413	2.618	0.116
	Within Groups	395.167	6	65.861		
	Total	4705.500	31			
Hematocrit (%)	**Between Groups**	631.737	25	25.269	4.079	0.043
	Within Groups	37.172	6	6.195		
	Total	668.909	31			
Urea (mg/dl)	**Between Groups**	3135.302	25	125.412	3.530	0.061
	Within Groups	213.167	6	35.528		
	Total	3348.469	31			
Wbc (x 10^9/L)	**Between Groups**	186.729	25	7.469	6.089	0.016
	Within Groups	7.360	6	1.227		
	Total	194.089	31			
MCV (fL/red cell)	**Between Groups**	1122.447	25	44.898	5.767	0.018
	Within Groups	46.712	6	7.785		
	Total	1169.159	31			
Glucose (mg/dl)	**Between Groups**	24741.052	25	989.642	0.774	0.703
	Within Groups	7671.667	6	1278.611		
	Total	32412.719	31			
Plt (x 103/µL)	**Between Groups**	204286.469	25	8171.459	2.279	0.154
	Within Groups	21514.500	6	3585.750		
	Total	225800.969	31			

Table Description : Osmolality- Evaluated One Way Anova Test Between Other Parameters.
According to this table, higher serum osmolality was correlated with higher baseline creatinine (p<0.001), higher CRP (p=0.01), higher WBC (p=0.016), greater MCV (p=0.018); lower hematocrit (p= 0.043) and lower albumin (p<0.001). All these findings were considered as statistically significant.