T.C.
ERCİYES ÜNİVERSİTESİ
BİLİMSEL ARAŞTIRMA PROJELERİ
KOORDİNASYON BİRİMİ

KRİTİK HASTALARDA AKUT VE KRONİK DÖNEMDE VİTAMİN D DÜZEYİNİN DEĞERLENDİRİLMESİ VE KLİNİK PARAMETRELER ÜZERİNE ETKİSİ

Proje No: TSA-2016-6082

Proje Türü
Normal Araştırma Projesi

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OCAK 2017

KAYSERİ

TEŞEKKÜR

Bu çalışma "**TSA-2016-6082**" proje kodu ile Erciyes Üniversitesi Bilimsel Araştırmalar Koordinasyon Birimi tarafından desteklenmiştir.

İÇİNDEKİLER

ÖZET

Kritik hastalarda akut ve kronik dönemde Vitamin D düzeyinin değerlendirilmesi ve klinik parametreler üzerine etkisi

Amaç: Kritik hastalarda akut ve kronik dönemde Vitamin D düzeyinin değerlendirilmesi ve klinik parametreler üzerine etkisini araştırmaktır.

Materyal ve Method: Bu çalışma prospektif olarak Erciyes Üniversitesi Tıp Fakültesi Medikal Yoğun Bakım ünitesinde yapılmıştır. Çalışmaya 18 yaş ve üzeri 48 saatten daha fazla yoğun bakımda tedavi gören hastalar alındı. Hastalardan baseline, 3.gün, 7.gün ve 10.günlerde D vitamin seviyesi çalışıldı.

Bulgular: Çalışmaya 62 hasta alındı. Hastaların 30'u erkek (%48), 32'si ise kadın (%52) idi. Yaş ortalaması 53±20 yıl idi. Yoğun bakım ünitesine en sık yatış nedenleri solunum yetmezliği (%39) ve sepsis/septik şok (%29) idi. APACHE II skoru ortalama 15±8 olarak hesaplandı. Hastaların baseline, üçüncü ve yedinci gün D vitamin düzeyleri sırasıyla median 12,8 (2.80-104,0) mcg/L, 8.35 (1.80-96.30) mcg/L, 9.30 (4.60-37.00) mcg/L idi. Baseline D vitamini seviyesi düşüklüğü %84, 3. Gün D vitamini seviyesi düşüklüğü ise %90 oranında tespit edildi. Yoğun bakım, hastane, 1 aylık ve 6 aylık mortalite sırasıyla %27, %36, %39 ve %45 oranında bulundu. Yoğun bakım mortalitesi ile baseline, 3 gün ve 7 gün D vitamin seviyesi arasında ilişki saptanmadı (sırasıyla p:0,494, p:0,540, p:0,7). Hastane mortalitesi ile baseline, 3 gün ve 7 gün D vitamini seviyesi arasında ilişki saptanmadı (sırasıyla p=0,678, p=0,746, p=0,7). Bir aylık mortalite ile baseline, 3 gün ve 7 gün D vitamini seviyesi arasında ilişki saptanmadı (sırasıyla p=0,734, p=0,756, p=0,7). Altı aylık mortalite ile baseline, 3 gün ve 7 gün D vitamini seviyesi arasında ilişki saptanmadı (sırasıyla p= 0,872, p= 0,906, p= 0,7). Mekanik Ventilatör gün sayısı 4±5 gün, yoğun bakım gün sayısı 7±5 gün, hastanede kalış gün sayısı 12±9 gün idi.

Sonuç: Yoğun Bakım Ünitesi'ne hastaları ilk kabulde ve takiplerinde D vitamini seviyesi düşük olarak bulundu. D vitamini seviyesi ile mortalite arasında ilişki tespit edilmedi.

Anahtar Kelimeler: D vitamini, kritik hastalık, mortalite

ABSTRACT

EVALUATION OF VITAMIN D LEVEL IN ACUTE AND CHRONIC RELEVANT IN CRITICAL DISEASES AND EFFECT ON CLINICAL PARAMETERS

Objective: To assess vitamin D levels during acute and chronic disease periods in critically ill patients and to investigate its effect on clinical parameters.

Material and method: This prospective study was conducted at medical Intensive Care Unit of Erciyes University, Medicine School. The study included patients aged≥18 years who received care in medical ICU for >48 hours. Vitamin D level was measured at baseline and on the days 3, 7 and 10.

Results: Overall, 62 patients were recruited to the study, including 30 men (48%) and 32 women (52%). Mean age was 53±20 years. The most common cause of ICU admission was respiratory failure (39%), followed by sepsis/septic shock (29%). APACHE II score was calculated as 15±8. Median vitamin D levels at baseline and on the days 3 and 7 were 12.8 (2.80-104.0) mcg/L, 8.35 (1.80-96.30) mcg/L, 9.30 (4.60-37.00) mcg/L, respectively. Low vitamin D level was detected in 84% of patients at baseline whereas in 90% of patients on the day 3. ICU mortality, in-hospital mortality, 30-day mortality and 6-month mortality were found to be 27%, 36%, 39% and 45%, respectively. No significant correlation was detected between ICU mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.494, p: 0.540, p: 0.7, respectively). No significant correlation was detected between in-hospital mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.678, p: 0.746, p: 0.7, respectively). No significant correlation was detected between 30-days mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.734, p: 0.756, p: 0.7, respectively). No significant correlation was detected between 6-months mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.872, p: 0.906, p: 0.7, respectively). Day of mechanical ventilation was 3±5 days. Length of hospital stay was 12±9 days while length of ICU stay was 7±5 days.

Conclusion: Vitamin D level was found to be low at admission to ICU and during follow-up. No significant correlation was detected between vitamin D level and mortality.

Key words: Vitamin D, critical illness, mortality

INTRODUCTION

Vitamin D (vit D) is a fat-soluble vitamin, plays an important role in bone metabolism, it is a steroid hormone which has pleiotropic effects by this property it regulates immunity, cell proliferation, apoptosis, and angiogenesis. There is a close relationship between vit D insufficiency and systemic disorders result in morbidity and mortality (1,2). Vit D insufficiency is common in hospitalized patients and especially in critically ill patients (3,4)

In critically ill patients the incidence of insufficiency has been reported varies between 26% to 82% (5,6). In intensive care unit (ICU) patients; insufficiency of vit D may worsen immune and metabolic dysfunctions and result in worse outcomes (6,7).

The aim of this study was to evaluate vit D status in our single center ICU patients and to demonstrate the relationship between vit D status and mortality rate.

PATIENTS AND METHODS

This prospective observational study conducted in a 18-bed medical ICU at Erciyes University Hospital, Kayseri (38,73122ºN and 35,478729 ºE, mean elevation of 1054 metres-3458 ft), Turkey. Tertiary reference center ICU in which study was conducted, has an annual occupancy of 600 patients.The study has been approved by the Institutional Ethical Committee (date: 23.05.2014, number: 2014/341). Patients consecutively admitted to the ICU between November 2014 and December 2015 were included to the study. All patients informed about the study, for conscious patients information directly given to her/him, for unconscious ones families were informed. Patients or their legally authorized representatives provided written informed consent.

Inclusıon criteria: The patients above 18 years of age, patients suspected to stay more than 48 hours in ICU.

Exclusion criteria: Patients with chronic renal failure, chronic liver disease, granulomatous diseases hereditary phosphate-related diseases, vitamin D resistant ricketsia,oncogenic osteomalasia, pregnant patients, patients who stayed in the ICU less than 48 hours, were aged below 18 years, were using drugs related to bone metabolism.

Blood samples for vit D levels were drawn in the first 24 hours of ICU admission and were centrifuged at 2000 g for 5 minutes. Sera protected from light and were stored at -80 ºC until

analysis. Serum vit D 25 (OH)D levels were measured by radioimmunoassay (ZİVAK Pandem-Gold LC-MS/MS) and levels below 20 ng/mL (D Vitamini referans aralığı (bizim lab) kış:10-60 mcg/L, yaz:20-120 mcg/L)ben kılavuzlardaki standart değeri yazdım bizdeki referans değer neyse o yazılmalı,bizdeki değer in birimide mcg/L ama çalışmalar hep ng olarak verilmiş.Aslında iki değer aynı,ng daha formal yazım mı acaba?? Ng yazalım) were defined to be insufficient.

The following data was recorded and analyzed in the study: Demographics; admission acute physiology and chronic health evaluation (APACHE) II score; sequential organ failure assessment (SOFA) score in 1-3-7 days ; Glasgow coma scale (GCS); underlying diseases; cause of admission to ICU, mechanical ventilation day, renal replacement therapy need, nosocomial infections, the length of ICU stay, the length of hospital stay, 30 days and 6 months mortality.

Statistical Analysis

SPSS software (SPSS version 15.0) was used for statistical analysis. Shapiro-Wilk's test was used; also histogram and q-q plots were examined to assess the data normality. Levene's test was used to test variance heterogeneity. To compare the differences between groups, a two-sided independent samples t test and Mann-Whitney U test was performed. Also, one-way repeated measures analysis of variance and Friedman tests were used for between time comparisons.

RESULTS

In this study 62 patients were recruited, including 30 men (48%) and 32 women (52%). Mean age was 53±20 years. Demographic and clinical characteristics are given in Table 1. The most common cause of ICU admission was respiratory failure (39%), followed by sepsis/septic shock (29%). APACHE II score was calculated as 15±8. Median vitamin D levels at baseline and on the days 3 and 7 were 12.8 (2.80-104.0) mcg/L, 8.35 (1.80-96.30) mcg/L, 9.30 (4.60-37.00) mcg/L, respectively. Low vitamin D level was detected in 84% of patients at baseline whereas in 90% of patients on the day 3. ICU mortality, in-hospital mortality, 30-day mortality and 6-months mortality were found to be 27%, 36%, 39% and 45%, respectively. No significant correlation was detected between ICU mortality and vitamin D levels at baseline

and on the days 3 and 7 (p: 0.494, p: 0.540, p: 0.7, respectively). No significant correlation was detected between in-hospital mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.678, p: 0.746, p: 0.7, respectively). No significant correlation was detected between 30-days mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.734, p: 0.756, p: 0.7, respectively). No significant correlation was detected between 6-months mortality and vitamin D levels at baseline and on the days 3 and 7 (p: 0.872, p: 0.906, p: 0.7, respectively). Day of mechanical ventilation was 3±5 days. Length of hospital stay was 12±9 days while length of ICU stay was 7±5 days.

DISCUSSION

Vitamin D sufficiency means that circulating 25 (OH) D level satisfies physiologic needs. In the general population, a minimum 25 (OH) D level of 20 ng/mL (50 nmol/L) is necessary for (6) the bone and mineral health, and 30–40 ng/mL (75– 100 nmol/L) is necessary to maintain muscle strength and immune functions (8). Unfortunatelly there is no certain defined vitamin D level for critically ill patients and definitions used in the general population have applied in critically ill patients in most of studies (4-6). Therefore, we used 25 (OH) D level (20 mcg/L) as a cutoff to define insufficiency in our ICU patients. Prevalence of vit D insufficiency is 26% to 82% in critically ill patients. It is reported that prevalence in ICU is higher than that of patients in general medical wards (5,6). In our prospective observational study, we demonstrated that baseline 84 % of patients were vit D insufficient. Baseline The median 25 (OH)D level was 12.80 mcg/L (range2.80-104.00). Such a high ratio may be due to older age, sun avoidance, low dietary intake, comorbidities (9-11). Even the mean age of the patients in our study is 53 years old, it is under geriatric level, chronic, severe underlying diseases or comorbidities can be the one reason of low vitamin D level in our medical ICU patients. Second, vitamin D levels obtained within 24 hours on admission this level can be the reflection of preadmission insufficiency. For this reason we sample 25 (OH) D levels sequentially and we follow up vit D levels during ICU stay. It is expected that 25 (OH) D levels would be declined further during ICU stay because we didnt give any supplement, sunlight exposure were also absent (5,9-11).

We found that level of 25 (OH) D declined from 12.8 mcg/L to 8.35 mcg/L in 3rd day. Interaction with medications, abnormalities in gastrointestinal function and the amount of fluid resuscitation can be the cause of this decline (9-11).Contrary to the study conducted by McKinney et al., we did not find any correlation between 25 (OH) D insufficiency and length

of ICU stay (LOS) (10). In the study conducted by van den Berghe et al., vit D levels were lower among non survivors (12). Lee et al. showed threefold increase in mortality rate in vit D insufficient patients compared to sufficient ones (3). The increased mortality in case of vitamin D deficiency may be due to changes in calcium metabolism and/or immune and endothelial cell dysfunction (13,14). Also Contrary to Braun et al.(15) and the other all studies we did not find any correlation between 25 (OH) D insufficiency and short-long term mortality. Perhaps vitamin D insufficiency maybe a helper but not a real risk factor for mortality. In our study APACHE II score was 15±8 and at admission, mean SOFA score was 4.0 ±3 and in 3rd day SOFA was 3.5± 3.4 which means that our patients were not so severe. We estimated that if our patients were in higher APACHE II and SOFA score mortality would be effected.

Vitamin D regulates immune system, insufficiency leads to immune dysregulation result in increased susceptibility to nosocomial infections such as ventilator associated pneumonia; increase the duration and severity of systemic inflammatory response and multiorganfailure (16-18). Most of studies demonstrate that current support is not adequate and high doses of vit D restored sufficiency within several days without complications in critically ill patients and approximately 400–600 units of vit D are provided daily in standard nutritional support (19) . In our study also in 7th day of admission vitamin D level is higher than 3rd day level. This increase may be due to given vit D with standart product.

Our study has several limitations. It was a single center study with a small sample size; therefore, our study results can not be generalize. It was conducted in a medical ICU and cannot be generalized to cardiac, surgical, or other ICUs.

In conclusion, vit D insufficiency is common in critically ill patients in our Medical Intensive Care Unit. Further multicenter studies with a larger sample size are required.

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Table 1:Patients baseline demographics and clinical characteristics

Variables	
Age, (± SD) (year)	53±20
Sex, n (%) Male Female	 30(48) 32(52)
Reason for ICU admission, n (%) Respiratory failure Sepsis/septic Shock Neurolojic disorder Intoxication Other	 24(39) 16(29) 5(8) 4(7) 13(21)
Glasgow Coma Score (± SD)	10.7±4
APACHE II score (± SD)	15.1±8
SOFA score day 1 (± SD)	4.0±3
SOFA score day 3 (± SD)	3.5±3
Baseline 25(OH)D level (mcg/L), (range)	12.80(2.80-104.00)
Third day25(OH)D level (mcg/L),(range)	8.35(1.80-96.30)
Seventh day25(OH)D level (mcg/L),(range)	9.30(4.60-37.00)
Calcium (mg/dL), (± SD)	8.3±1
Calcium, ionized (mmol/L), (± SD)	0.66±0.2
Phosphoruslevel (mg/dL), (± SD)	3.4±1
Albumin (mg/dL), (± SD)	3.1±0.8
Baseline CRP (mg/L), (range)	113 (3.45-420)
Baseline procalsitonin (ng/mL), (range)	0.63(0.005-151)
Vasopressor usage, n(%)	14(23)
Renal replasman therapy, n (%)	6(10)
New ınfection, n(%)	11(18)
Invasive mechanical ventilation, n (%)	33(53)
Length of ICU stay, (days)(range)	7±5
Length of hospital stay, (days)(range)	12±9
ICU mortality, n(%)	17(27)
Hospital mortality, n(%)	22(36)
30-day mortality, n(%)	24(39)
6-months mortality, n(%)	28(45)

APACHE: acute physiology and chronic health evaluation, SOFA: sequential organ failure assessment
ICU: intensive care unit, CRP: C-reaktif protein