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Araştırma/*Research Article*

Age-Related Hemodynamic Effects of Long-term Use of Dexmedetomidine During NIV

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NIV Sırasında Uzun Süreli Deksmedetomidin Kullanımının Yaşa Bağlı Hemodinamik Etkileri

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ABSTRACT

Objective: *Sedation in the intensive care unit plays a key role in patient management as it helps suppress agitation, increases tolerance to stress, and facilitates medical interventions, such as noninvasive ventilation (NIV) Our purpose was to determine the long-term hemodynamic effects of dexmedetomidine in elderly patients with acute respiratory failure who require NIV.*
Methods: *We recorded the data concerning age, comorbidities, doses of dexmedetomidine, hemodynamic parameters, use of vasopressors and length of ICU stay, from the hospital electronic medical recor system Due to the possibility of causing hemodynamic instability in ICU, patients with reduced ventricular contractility, hypothermia, septic shock, endocrine pathologies and neurosurgery cases, were excluded from the study.*
Results: *The patients were evaluated in four age groups: Group I: 18-39 years; Group II, 40-64 years; Group III, 65-80 years, and Group IV, aged >80 years The patients in group IV were found to be at a higher risk for a decrease in MAP following onset of dexmedetomidine treatment (p=0.005*). Notably, most of the vasoactive agents were used in patients over 85 years old (54.2%, p=0.005). With increasing age hypotension and vasopressor needs were found to exhibit a corresponding augmentation.*
Conclusion: *Dexmedetomidine meets requirements for sedation during NIV in the ICU. Even without loading dose the drug can induce hemodynamic instability, therefore close monitoring is necessary. In elderly, dexmedetomidine should be started at the lowest possible dose and slowly titrated according to the patient's response.*

Keywords: *dexmedetomidine, elderly patient, noninvasive ventilation, sedation*

ÖZ

Amaç: *Yoğun bakım ünitesinde sedasyon ajitasyon ve strese yanıtını baskılamak ve non-invaziv ventilasyon gibi tıbbi müdahaleleri kolaylaştırmak açısından önemli rol oynar. Bu çalışmada amaç, yoğun bakımda akut solunum yetmezliği nedeniyle non-invaziv ventilasyon desteği alan hastalarda uzun süreli deksmedetomidin kullanımının yaşa bağlı hemodinamik etkilerini incelemek.*
Yöntem: *Hastane elektronik tıbbi kayıtlarından yaş, ek hastalık, deksmedetomidin dozları, hemodinamik parametreler, vazopressör kullanımı ve yoğun bakım kalış süresi gibi veriler kaydedildi. Azalmış ventriküler kontraktilite, hipotermi, septik şok, endokrin patolojiler ve beyin cerrahisi hastaları doğrudan hemodinamik instabiliteye neden olabileceklerinden çalışma dışı bırakıldı.*
Bulgular: *Hastalar dört grup halinde değerlendirildi: 18-39 (Grup I), 40-64 (Grup II), 65-80 (Grup III) ve >80 yaş (Grup IV). Seksen beş yaş ve üzerindeki ileri yaşlı hastaların deksmedetomidin başlangıcını takiben ortalama arter basıncında diğer gruplardan daha fazla azalma saptanmıştır (p=0.005*). Vazoaktif ajan kullanımı da aynı şekilde 85 yaş üstü olan hastalarda daha fazla görülmüştür (% 54,2, p=0,005). Yaş arttıkça, hipotansiyon ve vazopresör ihtiyaçlarının da arttığı saptanmıştır.*
Sonuç: *Deksmedetomidin yoğun bakımda NIV sırasında sedasyon gereksinimlerini karşılar. Yükleme dozu olmasa dahi hemodinamik dengesizlik gözlemlenebilir, bu nedenle yakın izlem gereklidir. Yaşlılarda deksmedetomidin mümkün olan en düşük dozda başlatılmalı ve cevaba göre titre edilmelidir.*

Anahtar kelimeler: *deksmedetomidin, yaşlı hasta, non-invazif ventilasyon, sedasyon*

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INTRODUCTION

Sedation in the intensive care unit (ICU) plays a key role in patient management as it helps suppress agitation, increases tolerance to stress, and facilitates medical interventions, such as non-invasive ventilation (NIV) [1]. During NIV, it is crucial to preserve upper airway patency, ensure the non-suppression of respiration, and reduce the perception of dyspnea; therefore, deep sedation is not necessary [2]. Given the foregoing requirements, dexmedetomidine is a good option for sedation in patients with acute respiratory failure who require NIV [3]. The safety of dexmedetomidine in short-term use has already been established. It has a predictable cardiovascular profile and, most of the time, hemodynamic changes improve without treatment [4]. Due to a decrease in their physiological capacity and altered pharmacodynamic responses, elderly people are more sensitive to the effects of medications[5]. Moreover, long-term use safety, especially in the elderly, has not been adequately studied. Given that the number of the elderly population is growing, this dearth of knowledge will continue to present medical personnel with a clinical challenge. Therefore, in this study, we aimed to determine the long-term hemodynamic effects of dexmedetomidine in elderly people with acute respiratory failure who require NIV.

MATERIAL and METHODS

This retrospective single-center observational study was performed on patients who received long-term dexmedetomidine infusion (>24) during NIV, due to respiratory failure, between April 1, 2017, and February 28, 2020. The study was approved by the Ethics Committee of Acibadem Mehmet Ali Aydinlar University, Istanbul, Turkey (2020-03/20). We reviewed the clinical course and collected data on age, comorbidities, doses of dexmedetomidine, hemodynamic parameters, use of vasopressors, and length of ICU stay, from the hospital electronic medical record. Due to the possibility of causing hemodynamic instability in ICU, patients with reduced ventricular contractility, hypothermia, septic shock, endocrine pathologies, and neurosurgery cases, were excluded from the study.

Patients were enrolled if they met the following criteria: age over 18 years; need of non-invasive ventilation under dexmedetomidine using more than 24 h of intensive care with no other analgesia and/or sedation. Exclusion criteria were: use of other sedative or analgesic agents during dexmedetomidine infusion period, use of the drug less than 24 h, need of endotracheal intubation.

At our hospital, routinely we administer dexmedetomidine as a continuous infusion at doses ranging from 0.2 to 1.5 mcg/kg/hour without loading, due to the possibility of sharp drops in hemodynamic parameters. For monitorization of sedation we use Richmond Agitation Sedation Scale (RASS) in combination with physiological parameters like heart rate, blood pressure, mimic, gesture, and perspiration. After 1 hour of initiation of dexmedetomidine infusion, if the sedative effect is not at the expected RASS level, the rate of infusion increases or decreases by 0.1 mcg/kg/hour. In cases of developing bradycardia, hypotension, or both, sedation gradually decreases or restarts. Vasoactive medications with corresponding doses are used when needed. Bradycardia is defined as heart rate<60 beats per minute[5], requiring modification of dexmedetomidine doses. Hypotension is defined as mean arterial pressure (MAP) less than 65 mm Hg. Hypobradycardia is defined as both heart rate and arterial pressure's decreases as defined.

Statistical Analyses

All statistical analyses were performed using IBM SPSS for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Data are presented as mean, standard deviation (SD), median and interquartile range (IQR), according to the distribution of the values.

Used tests were normality test (Shapiro Wilk), Descriptive statistics, Chi-square relationship test, Repeated Measures Analysis.

RESULTS

A total of 100 intensive care unit (ICU) patients were included in the study. The patients were divided into four groups: 18-39 (group I), 40-64 (group II), 65-80 (group III), and >80 years (group IV). The patients' demographic and clinical characteristics are shown

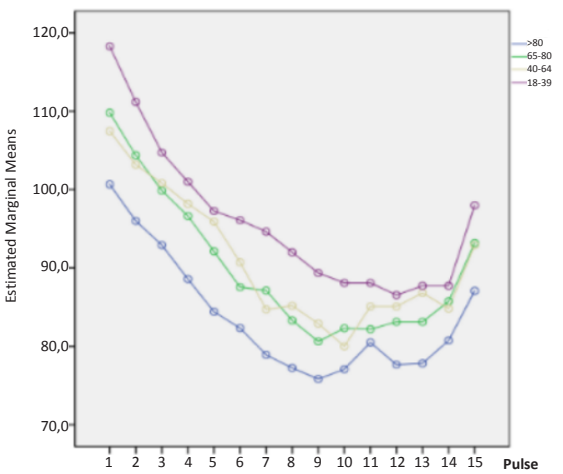
Table 1. Relationship analysis between the hemodynamic parameters of the patients and age groups.

	Group I n=22	Group II n=22	Group III n=32	Group IV n=24	P value
Age	18-39y	40-64y	65-80y	>80	0.000*
Comorbidities, n(%)					
Hypertension	0 (0%)	13 (59%)	25 (78%)	19 (79%)	0,031*
Diabetes	1 (4.5%)	2 (9%)	9 (28%)	8 (33%)	0,055
Chronic kidney	1 (4.5%)	2 (9%)	3 (9%)	7 (29%)	0,002*
Malignancy	3 (13.6%)	13 (59%)	18 (56%)	3 (12%)	0,014*
Others	0	9 (40%)	9 (28%)	7 (29%)	0.168
Bradycardia, n(%)	0(0.0)	2 (9.0)	6 (18.8)	4 (16.7)	0.005*
Hypotension, n(%)	2 (9.0)	8 (36.4)	12 (37.5)	13 (54.2)	0.127
Hypobradycardia, n(%)	0 (0.0)	2 (9.0)	3 (9.4)	2 (8.3)	0.005*
Vasopressor requirement, n(%)	2 (9.0)	8 (36.4)	12 (37.5)	13 (54.2)	
ICU duration, (%)					
0-7 days	45.5	27.3	25.0	41.7	0.175
7-14 days	45.5	36.4	31.3	25.0	
>14 days	9.1	36.4	43.8	33.3	

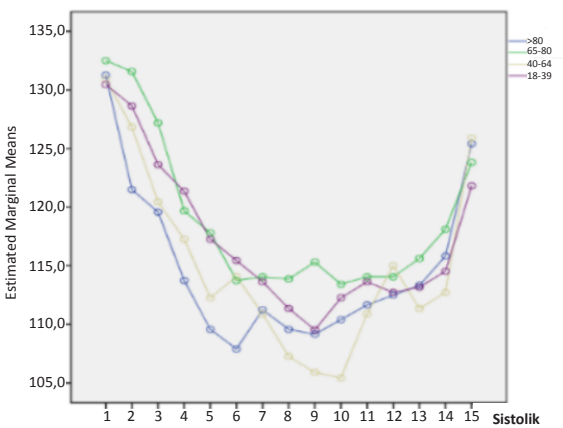
*Chi-square relationship test, *p≤0,05*

in Table 1. A continuous infusion of dexmedetomidine, median infusion time 71.5 (35-168).

When the results were evaluated, the patients in group IV were found to be at a higher risk for a decrease in MAP following dexmedetomidine initiation (p=0.005*). Notably, most of the vasoactive agents were used in patients over 80 years old (54.2%, p=0.005). As age increased, hypotension and vasopressor needs were found to exhibit a corresponding augmentation. Hypertension, diabetes mellitus, chronic kidney disease, and cancer were found to be the most common diseases among the elderly. There were significant differences in the groups with regard to the comorbidities, with the highest proportion of hypertension, diabetes mellitus, chronic kidney disease, and cancer noted in group IV. Group III accounted for a lesser proportion than group IV but the disparity was minimal. When the distribution chart of heart rate values by age group was evaluated, the highest decrease in heart rate was seen in group IV (Graph 1). However, this decrease was not statistically significant, and no difference was found between the age groups in terms of bradycardia (p=0.168). This result was similar to that of the distribution chart of mean arterial values by age group, with the largest decreases found in group IV (Graph 2). There was no significant relationship between bradycardia, hypobradycardia, ICU length of stay, and age group (p>0.05).



Graphic 1. Distribution chart of pulse values by age groups.



Graphic 2. Distribution chart of systolic blood pressure values by age groups.

DISCUSSION

Aging is associated with a decrease in physiological capacity and an increase of comorbidities, which can modify the response to all kinds of stress or the administration of sedatives. Nowadays the number of critically ill elderly patients is growing due to the aging of the population. Studies show that use of NIV in this group of patients is associated with decreased morbidity and mortality compared with invasive mechanical ventilation [6]. The poorer tolerance of the elderly to stress and associated complications is one of the indications for sedation. However, excessive sedation should be avoided. In these situations, dexmedetomidine comes to the fore, because it provides mild to moderate sedation without causing significant respiratory depression[3]. Moreover, it has been associated with improved patient communication with the hospital staff and a reduction in agitation and delirium [7]. Furthermore, NIV intolerance can increase the frequency of intubation [8].

Clear therapeutic goals and the potential adverse reactions should be considered when starting any sedation[4]. The cardiovascular responses to dexmedetomidine are generally predictable, and exaggerated drops can be minimized by starting at the lowest possible dose and titration based on response. As an alpha-2 agonist, it can increase the risk of hypotension and bradycardia [9]. Among healthy volunteers, dexmedetomidine was found to decrease the plasma levels of both noradrenaline and adrenaline[10]. Age alone is clearly a poor marker of the potential cause of hemodynamic instability, so elderly people will be more sensitive to all of the effects of the drug.

Our data support the growing body of literature indicating that hemodynamic parameters decrease as a significant side effect following dexmedetomidine initiation [11,12]. However, unlike other research, our study shows the difference in cardiovascular response among age groups. Cardiac reserve becomes less hemodynamically labile as an individual gets older. Therefore, the initiation of dexmedetomidine should be done with lower calculated doses and hemodynamic follow-up should be conducted more closely. Within 72 hours following dexmedetomidine initiation, older patients experienced the most substantial decrease in MAP (p=0.005). Likewise, the older patients needed more vasoactive support. In the younger patients, although there was a decrease in blood pressure and pulse after the initiation of dexmedetomidine, intervention was not required.

In our study, expectedly, comorbidities were found to increase with the advancement of age. The highest decrease in MAP following dexmedetomidine initiation was found in the elderly group, but it is difficult to say whether the hemodynamic lability develops due to age or comorbidities associated with it. For example, autonomic neuropathy is a major complication of diabetes mellitus and is reported to be associated with increased hemodynamic instability. It is worth mentioning that a relationship between autonomic dysfunction and hemodynamic response to anesthetics has been observed in diabetic patients[13]. Hemodynamic lability occurs more often in hypertensive patients [14]. Cancer patients are faced with more serious interactions and complications during anesthetic management. Central and autonomic nervous system toxicity and peripheral neuropathies, as well as cardiotoxicity, may occur in cancer patients who have received chemotherapy agents [15].

This study has several limitations. First, it is a retrospective study that involved the analysis of data from a single hospital. Thus, we cannot determine to what extent the results were affected by the efforts of clinicians to ameliorate hemodynamic instability, such as the administration of fluids. Second, we are unable to explain whether hypotension in elderly patients is caused by physiological changes or by the pathophysiological mechanism of comorbidities.

CONCLUSION

Dexmedetomidine meets requirements for sedation during NIV in the ICU. Even with no loading dose the drug can do haemodynamic instability, therefore close monitoring is necessary. It is useful to focus on non-pharmacological methods like decrease of environmental stimuli, early mobility, flexible family visitation policy and sleep hygiene. In elderly dexmedetomidine should be started at the lowest possible dose and slowly titrate according to the patient's response.

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