IJTMGH International Journal of Travel Medicine and Global Health

Int J Travel Med Glob Health. 2023 Jun;11(2):280-285
http://ijtmgh.com

doi 10.30491/IJTMGH.2023.396592.1362

Original Article Open Access

Assessment of the effect of Dexmedetomidine on peripheral oxygen saturation changes in patients with covid-19 pneumonia

Masoud Latifi-Pour[1], Majid Saeedi[2], Seyed Alireza Amouzegar Zavareh[3], Mostafa Baqerinasab[2], Seyed Mohammadreza Amouzegar Zavareh[4*]

[1] Chemical Injuries Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.
[2] Atherosclerosis Research Center and Faculty of Nursing, Baqiyatallah University of Medical Sciences, Tehran, Iran.
[3] Kashan University of Medical Sciences, Kashan, Iran.
[4] Arthrosclerosis research center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.

***Corresponding Author:** Seyed Mohammadreza Amouzegar Zavareh, Atherosclerosis research center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. Email: seyedmohammadrezaamoozgar@gmail.com, Tel: +989122016976

Received 2023-05-09; **Accepted** 2023-05-22; **Online Published** 2023-06-01

Abstract

Introduction: Sedative medications are widely used in intensive care unit patients. Decreased peripheral blood oxygen saturation (SPO2) is one of the common cases in patients with COVID-19. This study aimed to evaluate the effect of Dexmedetomidine on Peripheral oxygen saturation among COVID-19 pneumonia.

Methods: Sixty patients were randomly divided into two intervention groups (n=30) and control (n=30). Patients in the intervention group received dexmedetomidine with a bolus dose of 1 µ/kg/h for 10 minutes and then with a dose of 0.2 µ/kg/h to achieve a RASS score of -2 to +1. Patients in the control group received sedation drugs such as benzodiazepines, opium, or propofol according to the routine of the center. The well-known Richmond Stimulation and Sedation Scale (RASS) was used to evaluate patient sedation.

Results: Data analysis has shown that the changes in systolic and diastolic blood pressure and breathing rate are not significantly different between the two groups of patients (P>0.05). Patients in the intervention group have higher SPO2 compared to control group patients from 72 hours after starting Dexmedetomidine without any considerable adverse effect (P<0.01).

Conclusion: The potential sedation effect of dexmedetomidine can be attributed to the improvement in lung mechanics due to better relaxation in the thorax. Improvement in SpO2, and mental status (from agitated to calm) of patients which could be due to dexmedetomidine.

Keywords: COVID-19; Dexmedetomidine; peripheral oxygen saturation.

Citation: Latifi-Pour M, Saeedi M, Amouzegar Zavareh SA, Baqerinasab M, Amouzegar Zavareh SM. Assessment of the effect of Dexmedetomidine on peripheral oxygen saturation changes in patients with covid-19 pneumonia. Int J Travel Med Glob Health, 2023;11(2):280-285. doi: 10.30491/IJTMGH.2023.396592.1362.

Introduction

Patients with covid-19 pneumonia who admitted to the intensive care unit (ICU) usually require sedation to facilitate work of breathing and ventilatory support. Most of the existing sedative drugs carry the risk of side effects such as respiratory depression, confusion, and weakening of blood pressure, which may be harmful or even life-threatening to the patient [1-2].

Decreased peripheral blood oxygen saturation (SPO2) is one of the common cases in patients with COVID-19 [3]. The causes of SPO2 drop in these patients are psychological disorders such as depression, anxiety, shortness of breath following silent hypoxemia and disruption of pulmonary vasoregulation caused by endothelial damage of pulmonary capillaries and subsequent V/Q mismatch [3-8].

Dexmedetomidine is a relatively new alpha-2-adrenergic activating drug used for sedation in adult ICU patients. This drug may be used as an adjunct to anesthesia in intubated patients as well as for mild sedation in awake spontaneously breathing patients with or without non-invasive ventilation[4-10]. In addition to its sedative effect, dexmedetomidine also has analgesic and antiemetic effects. Compared to traditional sedatives and

Copyright © 2022 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

anesthetics, dexmedetomidine has very little effect on breathing, making it an ideal sedative for spontaneously breathing patients with impaired breathing [3, 8-12].

The aim of this study is that due to the proven effects of dexmedetomidine in controlled sedation with minimal effect of respiratory depression and increased hypoxic pulmonary vasoconstriction, which improves the ventilation/perfusion ratio and subsequently improves oxygen delivery, the use of this drug in improving SPO2 in Patients with COVID can be effective. This study was designed and implemented with the aim of investigating the effect of dexmedetomidine on improving SPO2 in patients with COVID.

Methods

This study is a randomized clinical trial that was conducted at Baqiyatallah Hospital in Tehran. This research was approved by the ethics committee of Baqiyatallah University of Medical Sciences and was conducted after obtaining the code of ethics (IR.BMSU.BAQ.REC.1401.010) and obtaining informed consent from the patient or the patient's legal representative.

Considering a moderate size effect of 0.3, a significant level of 0.05, and a power rate of 80%, sixty patients were randomly divided into two intervention groups (n=30) and control (n=30) using a random number table. Patients with a positive COVID-19 test, SPO2<90% and under non-invasive mechanical ventilation with a mask were included in the study. Patients with primary acute brain injury, neurological and mental disorders were excluded from the study. Age, sex, weight and co-morbidities including diabetes, blood pressure, heart disease, lung disease and kidney disease were evaluated and recorded. After being admitted to the ICU, all patients underwent oxygen therapy with an oxygen mask with a reservoir bag.

The well-known Richmond Stimulation and Sedation Scale (RASS) was used to evaluate patient sedation. RASS is one of the recommended criteria for assessing the sedation of Persian-speaking ICU patients with a suitable reliability coefficient. The validity and reliability of RASS has been proved by Sessler[5] and its validity in Iran in 2009[6]. The RASS scale ranges from -5 (unresponsive) to +4 (combative). The goal of sedation in this study is RASS -2 (mild sedation) to RASS +1 (restless). Patients were evaluated by RASS criteria at the beginning of admission to ICU, every 6 hours in the first 24 hours and up to 5 days daily.

Patients in the intervention group received dexmedetomidine with a bolus dose of 1 µ/kg/h for 10 minutes and then with a dose of 0.2 µ/kg/h in order to achieve a RASS score of -2 to +1. Patients in the intervention group were received dexmedetomidine as the only sedation agent. The use of benzodiazepines in this group is completely prohibited for the researcher, except in some special cases such as uncontrollable restlessness or delirium, convulsions and sedation for invasive interventions or in the case of simultaneous use of neuromuscular blocking drugs.

Dexmedetomidine was prescribed according to clinical need until non-invasive mechanical support or reaching the target RASS score without receiving medication. Patients in the control group received sedation drugs such as benzodiazepines, opium, or propofol according to the routine of the center.

Information was recorded if non-invasive ventilation, endotracheal intubation or other supportive measures were required. Data was analyzed by SPSS-26 software. Normality was assessed by kolmogorov smirnov test. A P-value less than 0.05 was considered for statistical significantly point. T-test, Mann-Whitney, Chi2 was used for comparison statistically between groups.

Results

The results of the table number one show the demographic information and co-morbidity diseases of the patients participating in the study. As table number one shows, the basic information between the groups are not statistically different and the two groups are statistically comparable.

Table 1. Demographic and co-morbidity data.

Variable		dex	control	P-value
Sex	Woman	13 (43.3)	12 (400)	0.793
	Man	17 (56.7)	18 (60)	
Age		5500±1106	5573±1354	0.162
Weight		83.93±1585	83.33±1273	0.801
DM		11 (36.7)	12 (40)	0.791
HTN		11 (36.7)	11 (36.7)	0.999
Cardiac D*		0 (0.0)	6 (20.0)	0.012
Pulmunaray D		0 (0.0)	2 (6.7)	0.246
Renal D		1 (3.3)	0 (0.0)	0.512
Nervous D		4 (13.3)	0 (0.0)	0.056

The results of Table No. 2, 3, and 4 show the changes in systolic blood pressure, diastolic blood pressure, and respiratory rate in the study groups, respectively. As shown, the changes in systolic and diastolic blood pressure and breathing rate are not significantly different between the two groups of patients.

Table 2. Systolic blood pressure variations in study groups.

Group		primary	Bolus doose	First 2H	Second 2H	Third 2H	Second 6H	Third 6H	Second 24H	Third 24H	Forth 24H	Fifth 24 H
dex	mean	135.46	134.43	131.63	124.73	124.76	129.13	125.55	124.96	118.68	117.13	118.44
	SD	22.43	22.12	17.86	14.91	14.50	17.17	13.11	12.02	12.06	12.95	11.66
control	mean	121.43	127.76	125.80	120.56	119.40	119.40	121.03	119.11	159.19	116.95	114.86
	SD	23.97	10.03	15.09	19.84	18.10	19.25	15.38	16.06	217.39	12.81	13.02
P_value		0.052	0.31	0.06	0.24	0.10	0.02	0.20	0.055	0.72	0.91	0.38

Table 3. Diastolic blood pressure variations in study groups.

Group		primary	Bolus doose	First 2H	Second 2H	Third 2H	Second 6H	Third 6H	Second 24H	Third 24H	Forth 24H	Fifth 24 H
dex	mean	82.96	82.83	81.73	77.63	77.50	77.53	77.51	76.82	75.48	72.79	74.75
	SD	11.45	11.77	8.87	11.22	10.10	11.05	10.55	9.21	9.71	10.77	11.38
control	mean	80.50	79.93	78.70	77.40	78.96	77.82	77.07	76.15	73.53	73.21	71.04
	SD	8.02	7.19	9.70	11.99	11.62	11.25	12.40	12.88	9.39	10.02	11.21
P_value		0.22	0.19	0.10	0.70	0.77	0.91	0.74	0.95	0.39	0.54	0.46

Table 4. Respiratory rate variations in study groups.

Group		primary	Bolus doose	First 2H	Second 2H	Third 2H	Second 6H	Third 6H	Second 24H	Third 24H	Forth 24H	Fifth 24 H
dex	mean	27.06	27.16	26.36	27.40	26.06	25.53	25.89	25.51	23.93	22.72	22.72
	SD	7.05	7.746	6.50	5.79	6.69	7.89	6.77	6.115	5.25	5.29	4.97
control	mean	27.63	28.50	28.33	28.56	27.90	26.03	26.07	25.53	25.34	24.00	25.86
	SD	6.58	7.573	6.61	7.08	8.19	6.64	6.05	8.05	6.13	6.08	6.83
P_value		0.82	0.60	0.23	0.68	0.44	0.95	0.69	0.67	0.27	0.51	0.07

Table number 5 shows the SPO2 variations in the time intervals of the study. As it is known, intervention group patients have higher SPO2 compared to control group patients from 72 hours after starting Dexmedetomidine, which is statistically significant.

Table 5. Peripheral oxygen saturation variation in study groups.

Group		primary	Bolus doose	First 2H	Second 2H	Third 2H	Second 6H	Third 6H	Second 24H	Third 24H	Forth 24H	Fifth 24 H
dex	mean	79.20	79.30	79.96	81.56	82.93	83.16	83.23	84.20	85.17	85.93	87.79
	SD	9.02	10.46	10.60	9.87	8.85	10.04	7.63	6.17	6.00	6.27	9.93
control	mean	80.5	81.60	80.26	79.73	78.30	79.16	83.00	83.19	82.30	81.69	83.69
	SD	7.90	8.35	11.07	9.41	12.16	14.11	9.33	7.00	7.65	7.75	6.05
P_value		0.446	0.953	0.366	0.140	0.242	0.835	0.617	0.202	0.075	0.003	0.002

Table No. 6 shows the changes in RASS scores in the study groups. As it is known, there is no statistically significant difference in RASS score between study groups.

Table 6. The RASS score variations in study groups.

group		R 0	R 1	R2	R3	R4	R5	R6	R7	R8	R9	R10
dex	mean	2.06	1.70	0.93	0.43	0.26	0.23	-0.03	0.03	0.24	0.17	0.104
	SD	1.01	1.17	1.20	1.04	1.14	1.07	1.14	0.68	0.78	0.88	0.93
control	mean	1.83	1.46	0.90	0.80	0.70	0.37	0.23	0.80	0.65	0.26	0.52
	SD	0.87	1.43	1.51	1.51	1.46	1.11	0.86	1.54	1.52	1.38	1.59
P_value		0.49	0.27	0.31	0.81	0.62	0.91	0.56	0.16	0.46	0.71	0.44

Three patients in the control group were intubated on the second and third days, and two patients died on the fourth day. All 3 patients were excluded from the study.

Eight patients in the intervention group were intubated on the second to third days, and 5 died on the fourth day of the study. All 8 patients of the intervention group were excluded from the study.

Discussion:

COVID is a well-known disease with severe hypoxemia that requires multidimensional measures. In this study, our patients received standard medical treatment approved by the Iranian Ministry of Health and palliative measures such as Prone Positioning, chest physiotherapy, etc.

Applying light sedation using non-benzodiazepine drugs to create optimal sedation in the long term is still a challenging and risky issue. According to the pharmacokinetics of dexmedetomidine due to having minimal effect on respiratory drive, onset of effect and fast elimination and rapid titration, this drug is an ideal and safe drug in patients with COVID and non-intubated[3].

This study was conducted with the aim of investigating the effect of dexmedetomidine on SPO2 changes in patients with COVID-19 and it was found that patients receiving dexmedetomidine had a higher average SPO2 compared to the control group since the third day. However, the Shehabi and colleagues has shown that early use of dexmedetomidine in mechanically ventilated patients did not improve outcomes compared with usual care[6].

Dexmedetomidine increases oxygenation at the physiological level. It is thought that the mechanism of hypoxemia in COVID-19 is a disturbance in pulmonary vasoregulation caused by endothelial damage of pulmonary capillaries and subsequent V/Q mismatch[7]. Recent studies have shown that dexmedetomidine improves the ventilation/perfusion ratio by increasing hypoxic pulmonary vasoconstriction and subsequently improves oxygen delivery[8,9].

The results of the present study showed that the average SPO2 up to 72 hours after the start of dexmedetomidine was not statistically different between the two groups. However, since 72 hours later, the

average SPO2 in the patients of the intervention group was lower compared to the control group, and this difference was statistically significant. In the study of Lee et al. and Mahmoodpoor et al., an improvement in oxygenation was observed in patients receiving dexmedetomidine almost from the third day of dexmedetomidine administration[10, 11].

The mechanism of the favorable pulmonary effects of dexmedetomidine is not yet clear, however, various mechanisms have been attributed to these effects[9]. Animal studies have shown that dexmedetomidine has bronchodilatory effects in histamine-mediated bronchospasms. On the other hand, studies have shown that dexmedetomidine reduces hypoxic pulmonary vasoconstriction caused by the inhibitory effects of inhaled anesthetics, increases the perfusion of lungs under ventilator, reduces oxidative stress, etc. By stimulating alpha-2B receptors in vascular smooth muscles, dexmedetomidine increases hypoxic pulmonary vasoconstriction and probably increases the ratio of ventilation to perfusion and subsequently improves oxygenation. On the other hand, dexmedetomidine can reduce the intrapulmonary shunt by increasing the level of nitric oxide in the blood. Some studies have also shown the effect of dexmedetomidine in reducing inflammatory processes and pulmonary protective effects[12].

Bradycardia is a known side effect with this drug, which is well and easily tolerated by the patients[13-15]. As the results of our study showed, the patients receiving dexmedetomidine did not experience a drop in systolic and diastolic blood pressure compared to the patients in the control group. Except on the fifth day of the study, when the patients in the intervention group had a lower respiratory rate, which was statistically significant, and this was the case when the patients did not suffer from bradypnea.

In this study, the RASS criterion was used to evaluate the level of sedation of patients. As stated in the results, despite the non-significance of the RASS score between the two groups, the RASS score was lower in the patients of the intervention group. In this study, the non-significance of the RASS score between the study groups can be attributed to the small number of statistical samples. The potential sedation effect of dexmedetomidine can be attributed to the improvement in lung mechanics due to better relaxation in the thorax. Improvement in SpO2, mental status (from agitated to calm) of patients which could be due to dexmedetomidine.

Conclusion

The potential sedation effect of dexmedetomidine can be attributed to the improvement in lung mechanics due to better relaxation in the thorax. Improvement in SpO2, mental status (from agitated to calm) of patients which could be due to dexmedetomidine.

Research Highlights

What Is Already Known?

Dexmedetomidine is a relatively new alpha-2-adrenergic activating drug used for sedation in adult ICU patients. Decreased peripheral blood oxygen saturation (SPO2) is one of the common cases in patients with COVID-19.

What Does This Study Add?

COVID-19 patients in the dexmedetomidine group have higher SPO2 compared to control group patients from 72 hours after starting treatment without any considerable adverse effect.

Conflict of interest

We declare that there is no conflict of interest in this study.

Ethical Approval

This research was approved by the ethics committee of Baqiyatallah University of Medical Sciences and was conducted after obtaining the code of ethics (IR.BMSU.BAQ.REC.1401.010) and obtaining informed consent from the patient or the patient's legal representative.

Funding/ Support

None.

Authors' Contributions

Design and concepts: Masoud Latifi-Pour, Seyed Mohammadreza Amouzegar Zavareh; Data gathering: Masoud Latifi-Pour, Majid Saeedi, Seyed Alireza Amouzegar Zavareh, Mostafa Baqerinasab, Seyed Mohammadreza Amouzegar Zavareh; Data analysis: Masoud Latifi-Pour, Majid Saeedi, Seyed Alireza Amouzegar Zavareh, Mostafa Baqerinasab, Seyed Mohammadreza Amouzegar Zavareh; Writing and editing: Masoud Latifi-Pour, Majid Saeedi, Seyed Alireza Amouzegar Zavareh, Mostafa Baqerinasab, Seyed Mohammadreza Amouzegar Zavareh.

References:

1. Callaway E., Cyranoski D., Mallapaty S., Stoye E., Tollefson J. The coronavirus pandemic in five powerful charts. *Nature.* 2020;579:482–483. doi: 10.1038/d41586-020-00758-2
2. Vaduganathan M., Vardeny O., Michel T., McMurray J.J.V., Pfeffer M.A., Solomon S.D. Renin–angiotensin–aldosterone system inhibitors in patients with Covid-19. N Engl J Med. 2020;382:1653–1659. doi: 10.1056/NEJMsr2005760.
3. Akhtar M H, Haleem S, Tauheed N, et al. (January 19, 2023) Dexmedetomidine as Conduit for Non-Invasive Ventilation (NIV) Compliance in COVID-19 and Chronic Obstructive Pulmonary Disease (COPD) Patients in Intensive Care Unit (ICU) Setting: Case Series . Cureus 15(1): e33981. doi: 10.7759/cureus.33981.
4. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP, Elswick RK. The Richmond Agitation–Sedation Scale: validity and reliability in adult intensive care unit patients. American journal of respiratory and critical care medicine. 2002 Nov 15;166(10):1338-44. doi: 10.1164/rccm.2107138.

5. tadrisi s d S D, madani s j S J, farmand f ف, ebadi a ع, karimi zarchi a a A A, saghafinia م, et al . Richmond agitation–sedation scale validity and reliability in intensive care unit adult patients Persian version. jccnursing 2009; 2 (1) :15-21 (Persian version).

6. Shehabi Y, Howe BD, Bellomo R, Arabi YM, Bailey M, Bass FE, Bin Kadiman S, McArthur CJ, Murray L, Reade MC, Seppelt IM. Early sedation with dexmedetomidine in critically ill patients. New England Journal of Medicine. 2019 Jun 27;380(26):2506-17. doi: 10.1056/NEJMoa1904710.

7. Ghasemzadeh B, Azizi B, Azemati S, Bagherinasab M. The effects of dexmedetomidine prescription in paediatric patients with pulmonary hypertension under congenital heart surgery. Acta Medica Iranica. 2020 Jul 28:171-6. doi: 10.18502/acta.v58i4.3922

8. Ammar MA, Sacha GL, Welch SC, Bass SN, Kane-Gill SL, Duggal A, Ammar AA. Sedation, analgesia, and paralysis in COVID-19 patients in the setting of drug shortages. Journal of intensive care medicine. 2021 Feb;36(2):157-74. doi: 10.1177/0885066620951426.

9. Magoon R. Pulmonary vasculature in COVID-19: mechanism to monitoring!. Korean Journal of Anesthesiology. 2021 Apr 1;74(2):186-7. doi: 10.4097/kja.20536

10. Lee S. Dexmedetomidine: present and future directions. Korean journal of anesthesiology. 2019 Aug 1;72(4):323-30. Doi: 10.4097/kja.19259

11. Mahmoodpoor A, Ekrami E, Soleimanpour H. Dexmedetomidine: An all sedation-in–one drug in critically ill patients with covid-19. Pharmaceutical Sciences. 2020 Nov 30;26(Covid-19):S80-1. doi: 10.34172/PS.2020.53

12. Flanders CA, Rocke AS, Edwardson SA, Baillie JK, Walsh TS. The effect of dexmedetomidine and clonidine on the inflammatory response in critical illness: a systematic review of animal and human studies. Critical Care. 2019 Dec;23(1):1-1. doi: 10.1186/s13054-019-2690-4

13. Barron AJ, Zaman N, Cole GD, Wensel R, Okonko DO, Francis DP. Systematic review of genuine versus spurious side-effects of beta-blockers in heart failure using placebo control: recommendations for patient information. International journal of cardiology. 2013 Oct 9;168(4):3572-9. doi: 10.1016/j.ijcard.2013.05.068

14. Banerjee D, Reddy KR. Safety and tolerability of direct-acting anti-viral agents in the new era of hepatitis C therapy. Alimentary pharmacology & therapeutics. 2016 Mar;43(6):674-96. doi: 10.1111/apt.13514.

15. Haider KM, Plager DA, Neely DE, Eikenberry J, Haggstrom A. Outpatient treatment of periocular infantile hemangiomas with oral propranolol. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2010 Jun 1;14(3):251-6. doi: 10.1016/j.jaapos.2010.05.002.