Ito et al. Renal Replacement Therapy (2018) 4:54
https://doi.org/10.1186/s41100-018-0194-3

Renal Replacement Therapy

CASE REPORT Open Access

Sleep apnea syndrome caused lowering of cerebral oxygenation in a hemodialysis patient: a case report and literature review

Kiyonori Ito[1], Susumu Ookawara[1*], Mariko Fueki[2], Sojiro Imai[2], Takashi Hattori[2], Satoshi Kiryu[2], Yukari Sugai[3], Noriko Wada[3], Mitsutoshi Shindo[1], Yasushi Ohnishi[4], Noriaki Iino[5], Kaoru Tabei[4] and Yoshiyuki Morishita[1]

Abstract

Background: Sleep apnea syndrome (SAS) is a sleep disturbance, which is frequently comorbid in dialysis patients. SAS induces hypoxia, and therefore, systemic and cerebral oxygenation would be low. Near-infrared spectroscopy (NIRS) has recently been used to measure regional saturation of oxygen (rSO_2), as a marker of tissue oxygenation. Although cerebral rSO_2 was measured in patients in various clinical settings, few reports have previously shown the associations of changes in cerebral rSO_2 and systemic oxygenation using measurement of peripheral arterial oxygen saturation (SpO_2) in patients undergoing hemodialysis (HD) with SAS. We herein report a first HD case with SAS-induced reduction in cerebral oxygenation during sleep.

Case presentation: A 74-year-old woman underwent HD therapy for 1 month, because of advanced CKD caused by hypertension and obesity. In addition, she was diagnosed with obstructive sleep apnea with polysomnography about 4 years prior. Her apnea-hypopnea index (AHI) was 77.5 per hour, and therefore, continuous positive airway pressure (CPAP) was started. Thereafter, her AHI was improved to 3 to 6 per hour. However, she discontinued CPAP therapy at HD initiation. Since her oxygenation without CPAP would deteriorate, we evaluated her SpO_2 and cerebral rSO_2 by NIRS monitoring during sleep. We confirmed the deterioration in cerebral rSO_2 according to the SpO_2 decrease, and furthermore, the improvement in cerebral rSO_2 was apparently delayed even after the improvement in her SpO_2. The patient's cerebral oxygenation under CPAP therapy could not be evaluated because she refused to receive CPAP therapy after HD initiation. Therefore, as a comparison, we evaluated a 69-year-old male HD patient without SAS and found that in contrast to a patient with SAS, his SpO_2 and cerebral rSO_2 were maintained throughout sleep.

Conclusion: We observed deterioration in cerebral oxygenation during sleep in addition to a decrease in systemic oxygenation in a patient with SAS undergoing HD. Real-time cerebral NIRS monitoring during sleep might be a useful method for detection of SAS.

Keywords: Cerebral oxygenation, Sleep apnea syndrome, Hemodialysis, Regional saturation of oxygen (rSO2), Near-infrared spectroscopy (NIRS)

* Correspondence: su-ooka@hb.tp1.jp
[1]Division of Nephrology, First Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, 1-847 Amanuma-cho, Omiya-ku, Saitama 330-8503, Japan
Full list of author information is available at the end of the article

Background

Sleep apnea syndrome (SAS) is a sleep disturbance, which is frequently comorbid in dialysis patients [1, 2]. SAS induces hypoxia during apnea, and therefore, systemic and cerebral oxygenation would be low in these patients. However, few reports have examined regarding the changes in cerebral oxygenation during sleep in patients with SAS. Near-infrared spectroscopy (NIRS) has recently been used to measure regional saturation of oxygen (rSO_2), as a marker of tissue oxygenation. In particular, cerebral rSO_2 was measured in patients in various clinical settings, including hemodialysis (HD) patients [3–8]. It would be considered important to maintain cerebral rSO_2 levels because that low cerebral rSO_2 has been associated with cognitive impairment in patients with chronic kidney disease (CKD) [5, 8] and poor neurologic outcomes in post-cardiac arrest patients [7]. We aimed to examine the associations between changes in cerebral rSO_2 and those in systemic oxygenation using the measurement of peripheral arterial oxygen saturation (SpO_2%) in a patient undergoing HD with SAS.

Case presentation

A 74-year-old woman underwent HD therapy for 1 month, because of advanced CKD caused by hypertension and obesity. In addition, she was diagnosed with obstructive sleep apnea (OSA) with polysomnography about 4 years prior. Her apnea-hypopnea index (AHI) was 77.5 per hour and the arousal index was 76.1 per hour. Therefore, continuous positive airway pressure (CPAP) was started, and her AHI was improved to 3 to 6 per hour. However, she discontinued CPAP therapy at HD initiation. As systemic oxygenation would deteriorate without CPAP, we assessed her overnight SpO_2 using a pulse oximeter (PULSOX-Me300; TEIJIN PHARMA, Tokyo, Japan). Additionally, for the evaluation of cerebral oxygenation, we monitored cerebral rSO_2 using a regional saturation monitor (INVOS 5100c; Covidien Japan, Tokyo, Japan). Her vital sign and laboratory findings were as follows: blood pressure (BP) and pulse rate (PR) before evaluation; 127/71 mmHg, 76 beats/minute, BP and PR after evaluation; 121/59 mmHg, 80 beats/minute, hemoglobin (Hb): 9.5 g/dL, serum albumin (Alb); 2.7 g/dL, blood urea nitrogen (BUN): 48.2 mg/dL, serum creatinine (Cr): 4.13 mg/dL. Her physiological function examination findings were as follows: ejection fraction (EF): 60%, left ventricular systolic function was normal, mitral valve regurgitation was mild by echocardiography, and left and right carotid max intima-media thickness (IMT) were 1.1 and 1.1 mm, respectively by carotid ultrasonography. Cerebral rSO_2 level was evaluated as the rSO_2 ratio, which was defined as the ratio of rSO_2 at t (min) during sleep to the initial rSO_2 before bedtime [rSO_2 at t (min) during sleeping/initial rSO_2 before bedtime]. We confirmed the deterioration in cerebral rSO_2 according to the SpO_2 decrease in this HD patient with SAS. However, we could not directly comment on the influence of CPAP therapy on the improvement in systemic oxygenation because she refused to receive CPAP therapy after HD initiation. Therefore, as a comparison, changes in SpO_2 and cerebral rSO_2 were evaluated in a 69-year-old male HD patient without SAS. His vital sign and laboratory findings were as follows: BP and PR before evaluation 135/92 mmHg, 68 beats/minute, BP and PR after evaluation 148/100 mmHg, 61 beats/minute, Hb 11.1 g/dL, Alb 3.1 g/dL, BUN 55.7 mg/dL, and Cr 7.86 mg/dL. Results of his physiological function examination were as follows: EF: 71%, left ventricular systolic function was normal contraction, no valvular disease was noted by echocardiography, and left and right carotid IMT was 3.2 and 2.4 mm, respectively by carotid ultrasonography. Both patients provided informed consent before evaluation, and these examinations in each patient were performed on the day without HD therapy. The SpO_2 gradually decreased in patients with SAS from initiation to 3 h after sleep and then fell below 90%. According to the SpO_2 decrease during sleep, her cerebral rSO_2 simultaneously decreased; furthermore, the improvement in cerebral rSO_2 was apparently delayed even after the improvement in her SpO_2 (Fig. 1a). Her 3% Oxygen Desaturation Index was 19.0 times/hour by pulse oximetry. However, as shown in Fig. 1b, both his SpO_2 and cerebral rSO_2 ratio were maintained throughout sleep in the HD patient without SAS.

Discussion

We experienced a HD patient with SAS who showed a decrease in cerebral oxygenation in addition to a decrease in systemic oxygenation during sleep. In general, a decrease in systemic oxygenation would induce the deterioration of tissue oxygenation, including the brain. However, thus far, few reports have directly examined changes in cerebral oxygenation during sleep. Therefore, this case is a first report about nocturnal real-time monitoring of cerebral rSO_2 in a HD patient with SAS.

Sleep disorders, including SAS, are known as long-term complications in dialysis patients [1, 2]. Nocturnal hypoxia was associated with a poor prognosis for cardiovascular events [9], and patients with ischemic stroke have a high risk of obstructive sleep apnea, with lowest overnight SpO_2 values < 80% in more than half of observed patients [10]. Furthermore, in the clinical setting of HD therapy, cognitive impairment is common in patients undergoing HD and the pathogenesis of cognitive impairment would be associated with hemodynamic factors including changes in BP or anemia [11]. In particular, both intradialytic hypotension and anemia reportedly

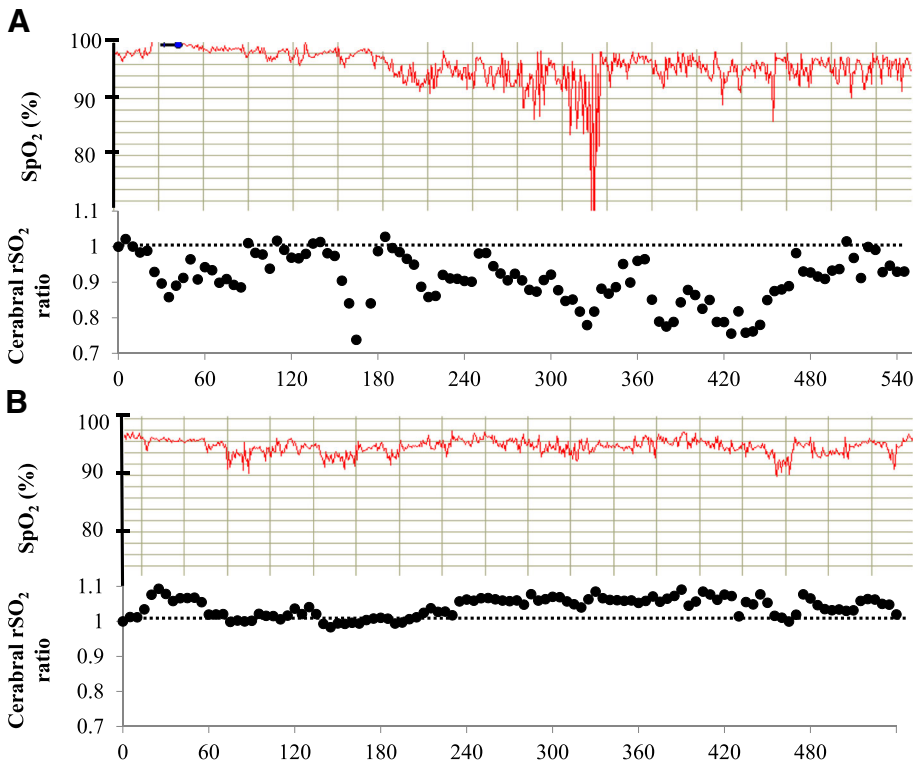

Fig. 1 Time course of SpO_2 and cerebral rSO_2 in a patient with obstructive SAS (**a**) and a patient without SAS (**b**). SpO_2 peripheral arterial oxygen saturation, rSO_2 regional saturation of oxygen, and SAS sleep apnea syndrome

induced the deterioration of cerebral oxygenation [12, 13]. In addition, the decrease in cerebral oxygen supply was associated with neuronal death, and hypoxia promoted the formation of amyloid ß peptide in experimental studies [14, 15]. Therefore, systemic oxygenation should be maintained to prevent worsening of cerebral oxygenation, which would be associated with the deterioration of cognitive function, in patients with SAS.

The measurement of cerebral rSO_2 by NIRS has recently been performed in various clinical settings, including cardiovascular surgery, pediatrics, and dialysis [3–8, 16–18]. We therefore, reviewed the literature for reports of cerebral rSO_2 values in dialysis patients (Table 1). Cerebral rSO_2 values in HD patients were lower than healthy control or non-dialysis patients [3, 8, 19–21] and were lower than peritoneal dialysis patients [22]. Therefore, the presence of renal dysfunction or dialysis therapeutic modality might influence the status of cerebral oxygenation. Furthermore, longer HD therapy itself might cause hypoxia of the brain because HD duration was negatively associated with cerebral rSO_2 [3, 19]. Regarding the association between cerebral rSO_2 and clinical parameters in maintenance HD patients, various factors, i.e., serum albumin, pH, Hb, and blood pressure, were related to cerebral rSO_2 [3, 13, 23]. Based on these previous reports, it would be important to maintain the nutritional status, and control Hb level and blood pressure in the clinical setting of HD therapy. On the other hand, it was also reported that there are little changes in cerebral rSO_2 during HD in spite of Hb increase induced by ultrafiltration in patients undergoing HD without intradialytic hypotension [6, 13, 20, 24]. However, thus far, there are few reports regarding the association between changes in systemic oxygenation and those in cerebral oxygenation in HD patients with or without SAS. Recently, evaluation of cerebral rSO_2 was reported to be useful for detection of SAS in addition to that using a pulse oximeter in children [18]. This report described that cerebral NIRS monitoring could detect SAS even in patients in whom SAS was ruled out with polysomnography, and AHI determined using cerebral rSO_2 had higher sensitivity for the detection of SAS compared with that using SpO_2 [18]. In HD patients with SAS, we noticed that a decrease in cerebral rSO_2 was observed more frequently than a decrease in SpO_2, and this result might be consistent with a previous report [18]. On the other hand, the HD patient without SAS in this study showed little changes in SpO_2 and cerebral rSO_2 during sleep. Therefore, in addition to the usefulness of polysomnography evaluation as a standard method for diagnosing SAS, cerebral rSO_2 measurement using NIRS might play an important role in the diagnosis of SAS in HD patients.

Table 1 Studies regarding cerebral oxygenation by near-infrared spectroscopy monitoring in dialysis patients

Authors	Year	Dialysis pattern	Number of patients	Main results about cerebral oxygenation	Reference
Prohovnik I, et al.	2007	HD	7	Cerebral rSO_2 in HD patients was lower than healthy control, and cerebral rSO_2 was negatively correlated with dialysis duration.	[19]
Papadopoulos G, et al.	2013	HD&PD	23 (HD), 9 (PD)	Cerebral rSO_2 in HD patients was lower than that in PD patients at preoperative condition.	[22]
Hoshino T, et al.	2014	HD	18	Cerebral rSO_2 in HD patients was lower than healthy control, and cerebral rSO_2 did not change during HD.	[20]
Ito K, et al.	2015	HD	54	Cerebral rSO_2 in HD patients was lower than healthy control, and cerebral rSO_2 was independently correlated with pH, dialysis duration, serum albumin, and diabetes mellitus.	[3]
Ito K, et al.	2017	HD	16	Cerebral rSO_2 in HD patients with severe anemia was lower than that in Hb well-controlled HD patients, and blood transfusion improved cerebral rSO_2.	[13]
MacEwen C, et al.	2017	HD	58	Cerebral rSO_2 was linearly dependent blood pressure below mean arterial pressure 60 mmHg.	[23]
Malik J, et al.	2017	HD	17	Cerebral rSO_2 was drop in the minimum value during the first 35 min, but cerebral rSO_2 did not change between before HD and after HD.	[24]
Ito K, et al.	2017	HD	108	Cerebral rSO_2 was correlated with aortic arch calcification by chest X-ray.	[4]
Matsukawa S, et al.	2017	HD	9	Cerebral rSO_2 in HD patients was lower than that in non-HD patients, although SpO_2 did not differ between HD and non-HD patients.	[21]
Kovarova L, et al.	2018	HD	39	Decreased cerebral rSO_2 was associated with cognitive impaired.	[5]
Ookawara S, et al.	2018	HD	44	Cerebral rSO_2 did not change during HD, and it was lower than liver rSO_2 from HD initiation to the end.	[6]

HD hemodialysis, *PD* peritoneal dialysis, *rSO_2* regional saturation of oxygen

Furthermore, the improvement in cerebral rSO_2 was apparently delayed even after the improvement in SpO_2 level (Fig. 1a). Although it is difficult to accurately state the mechanism of this phenomenon, we suspected two reasons regarding the difference between systemic and cerebral oxygenation improvement. First, NIRS monitoring was reported to have higher sensitivity for detecting SAS [18]. Therefore, the delay in cerebral oxygenation improvement might have the possibility to reflect the deep tissue oxygenation status, which was different from superficial arterial oxygenation status as shown in SpO_2 monitoring. Second, NIRS monitoring would mainly help observe venous oxygenation status (70–80%), against capillary (5%), or arterial blood (20–25%) [25]. On the other hand, SpO_2 monitoring could observe in the arterial blood oxygenation status. Brain cell would need the uptake of steady amount of oxygen into the cell according to the changes in oxygen supply in various conditions. In situations of decreased oxygen supply to brain such as severe anemia or hypoxic condition in SAS, cerebral rSO_2 would be low, which reflected the decrease of oxygen supply and the increase of oxygen extraction into the brain cell [13]. When hypoxic status in SAS transiently disappears during sleep, arterial oxygenation will be immediately improved, which lead to the SpO_2 increase. However, changes in oxygen extraction into brain cell might not be immediately normalized in response to the sudden increase of oxygen supply. As a result, there will be a lag time between the improvement in cerebral oxygenation and that of systemic oxygenation during sleep in this SAS patient. However, the mechanism of this phenomenon is yet not to be accurately clarified, and therefore, further studies are needed.

The use of CPAP improves systemic hypoxia in patients with SAS, and patients with OSA may have better outcomes under CPAP therapy through a decrease in the rate of recurrent myocardial infarction [26]. According to her prior medical records, the patient's AHI became relatively low under CPAP therapy compared to that without CPAP. Therefore, CPAP therapy would be effective in the prevention of systemic hypoxia during non-HD periods. Based on this result, cerebral oxygenation could be improved by CPAP therapy in patients with SAS in addition to the improvement of systemic oxygenation. However, further studies are needed to confirm the association between improvement in cerebral oxygenation and CPAP therapy in patients with SAS because we were unable to observe these associations in this study.

In conclusion, we observed cerebral oxygenation deterioration during sleep in addition to a decrease in systemic oxygenation in a patient undergoing HD with SAS. Furthermore, cerebral NIRS monitoring during sleep might be a useful method for the detection of SAS.

Acknowledgements
We thank the study participants and the clinical dialysis center staff in Minami-Uonuma City Hospital.

Funding
The authors declare that there is no funding related to this manuscript.

Availability of data and materials
All data analyzed during this study are included in this published article.

Authors' contributions
KI conceived and designed this study. KI, MF, SI, TH, SK, YS, NW, and MS performed this study. KI and OS analyzed the data. YO, NI, KT, and YM supervised the data collection and manuscript preparation. KI and OS drafted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Written informed consent was obtained from the patient after a detailed explanation of the objectives of the study, which was approved by the Institutional Review Board of Minami-Uonuma City hospital, Japan (H29-3). The patient anonymity should be preserved.

Consent for publication
For publication of this case report, agreement was obtained from the patient.

Competing interests
The authors declared that they have no competing interests.

Publisher's Note

Author details
[1]Division of Nephrology, First Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, 1-847 Amanuma-cho, Omiya-ku, Saitama 330-8503, Japan. [2]Department of Clinical Engineering, Minami-Uonuma City Hospital, Niigata, Japan. [3]Department of Nursing, Minami-Uonuma City Hospital, Niigata, Japan. [4]Department of Internal Medicine, Minami-Uonuma City Hospital, Niigata, Japan. [5]Department of Nephrology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami-Uonuma, Niigata, Japan.

Received: 20 September 2018 Accepted: 27 November 2018
Published online: 13 December 2018

References

1. Parker KP. Sleep disturbances in dialysis patients. Sleep Med Rev. 2003;7:131–43.
2. Forni Ogna V, Ogna A, Pruijm M, Bassi I, Zuercher E, Halabi G, et al. Prevalence and diagnostic approach to sleep apnea in hemodialysis patients: a population study. Biomed Res Int. 2015;2015:103686.
3. Ito K, Ookawara S, Ueda Y, Goto S, Miyazawa H, Yamada H, et al. Factors affecting cerebral oxygenation in hemodialysis patients: cerebral oxygenation associates with pH, hemodialysis duration, serum albumin concentration, and diabetes mellitus. PLoS One. 2015;10:e0117474.
4. Ito K, Ookawara S, Okochi T, Ueda Y, Kofuji M, Hayasaka H, et al. Deterioration of cerebral oxygenation by aortic arch calcification progression in patients undergoing hemodialysis: a cross-sectional study. Biomed Res Int. 2017;2017:2852514.
5. Kovarova L, Valerianova A, Kmentova T, Lachmanova J, Hladinova Z, Malik J. Low cerebral oxygenation is associated with cognitive impairment in chronic hemodialysis patients. Nephron. 2018;139:113–9.
6. Ookawara S, Ito K, Ueda Y, Miyazawa H, Hayasaka H, Kofuji M, et al. Differences in tissue oxygenation and changes in total hemoglobin signal strength in the brain, liver, and lower-limb muscle during hemodialysis. J Artif Organs. 2018;21:86–93.
7. Nishiyama K, Ito N, Orita T, Hayashida K, Arimoto H, Beppu S, et al. Regional cerebral oxygen saturation monitoring for predicting interventional outcomes in patients following out-of-hospital cardiac arrest of presumed cardiac cause: a prospective, observational, multicenter study. Resuscitation. 2015;96:135–41.
8. Miyazawa H, Ookawara S, Ito K, Ueda Y, Yanai K, Ishii H, et al. Association of cerebral oxygenation with estimated glomerular filtration rate and cognitive function in chronic kidney disease patients without dialysis therapy. PLoS One. 2018;13:e0199366.
9. Zoccali C, Mallamaci F, Tripepi G. Nocturnal hypoxemia predicts incident cardiovascular complications in dialysis patients. J Am Soc Nephrol. 2002;13:729–33.
10. Good DC, Henkle JQ, Gelber D, Welsh J, Verhulst S. Sleep-disordered breathing and poor functional outcome after stroke. Stroke. 1996;27:252–9.
11. Moeini M, Lu X, Avti PK, Damseh R, Belanger S, Picard F, et al. Compromised microvascular oxygen delivery increases brain tissue vulnerability with age. Sci Rep. 2018;8:8219.
12. Miyazawa H, Ookawara S, Tabei K. Aggravation of cerebral oxygenation due to intradialytic hypotension induced by blood volume reduction during hemodialysis: a case report. Ther Apher Dial. 2015;19:525–7.
13. Ito K, Ookawara S, Ueda Y, Miyazawa H, Kofuji M, Hayasaka H, et al. Changes in cerebral oxygenation associated with intradialytic blood transfusion in patients with severe anemia undergoing hemodialysis. Nephron Extra. 2017;7:42–51.
14. Peers C, Dallas ML, Boycott HE, Scragg JL, Pearson HA, Boyle JP. Hypoxia and neurodegeneration. Ann N Y Acad Sci. 2009;1177:169–77.
15. Peers C, Pearson HA, Boyle JP. Hypoxia and Alzheimer's disease. Essays Biochem. 2007;43:153–64.
16. Kobayashi K, Kitamura T, Kohira S, Torii S, Horai T, Hirata M, et al. Factors associated with a low initial cerebral oxygen saturation value in patients undergoing cardiac surgery. J Artif Organs. 2017;20:110–6.
17. Baik N, Urlesberger B, Schwaberger B, Avian A, Mileder L, Schmölzer GM, et al. Blood pressure during the immediate neonatal transition: is the mean arterial blood pressure relevant for the cerebral regional oxygenation? Neonatology. 2017;112:97–102.
18. Ullman N, Anas NG, Izaguirre E, Haugen W, Ortiz H, Arguello O, et al. Usefulness of cerebral NIRS in detecting the effects of pediatric sleep apnea. Pediatr Pulmonol. 2014;49:1036–42.
19. Prohovnik I, Post J, Uribarri J, Lee H, Sandu O, Langhoff E. Cerebrovascular effects of hemodialysis in chronic kidney disease. J Cereb Blood Flow Metab. 2007;27:1861–9.
20. Hoshino T, Ookawara S, Goto S, Miyazawa H, Ito K, Ueda Y, et al. Evaluation of cerebral oxygenation in patients undergoing long-term haemodialysis. Nephron Clin Pract. 2014;126:57–61.
21. Matsukawa S, Hamada M, Mizota T. Low preoperative regional cerebral oxygen saturation in hemodialysis patients. JA Clin Rep. 2017;3:13.
22. Papadopoulos G, Dounousi E, Papathanasiou A, Papathanakos G, Tzimas P. Cerebral oximetry values in dialyzed surgical patients: a comparison between hemodialysis and peritoneal dialysis. Ren Fail. 2013;35:855–9.
23. MacEwen C, Sutherland S, Daly J, Pugh C, Tarassenko L. Relationship between hypotension and cerebral ischemia during hemodialysis. J Am Soc Nephrol. 2017;28:2511–20.
24. Malik J, Kudlicka J, Lachmanova J, Valerianova A, Rocinova K, Bartkova M, et al. Tissue ischemia worsens during hemodialysis in end-stage renal disease patients. J Vasc Access. 2017;18:47–51.
25. Lemmers PMA, Toet MC, van Bel F. Impact of patent ductus arteriosus and subsequent therapy with indomethacin on cerebral oxygenation in preterm infants. Pediatrics. 2008;121:142–7.
26. Garcia-Rio F, Alonso-Fernández A, Armada E, Mediano O, Lores V, Rojo B, et al. CPAP effect on recurrent episodes in patients with sleep apnea and myocardial infarction. Int J Cardiol. 2013;168:1328–35.