Relationship between Asynchronies and Sleep Disruption in Mechanically Ventilated Patients: a prospective cohort study.

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Abstract

Mechanically ventilated (MV) patients in the Intensive Care Unit (ICU) are highly susceptible to sleep disruption. Several studies in the last 15 years have demonstrated an extremely poor sleep quality and abnormal sleep pattern evaluated by polysomnography (PSG) devices (the gold standard method for evaluating sleep quality and quantity).

Patient-ventilator interaction is frequently poor leading to asynchronies of varied type and consequences. Moderate-to-severe asynchronies are associated with longer mechanical ventilation, weaning failure and mortality.

The goal of this study is to look for an association between poor sleep quality and patient-ventilator asynchronies.

This study is an observational, physiological study investigating sleep quality and quantity in 50 MV patients by recording modified PSG (Prodigy. CerebraHealth) at night while continuously monitoring 24h/day of patient-ventilator interaction (BetterCare system).

Background:

Sleep is a natural condition that humans need for homeostasis maintenance. Hospitalized patients frequently suffer sleep disruption due to medical conditions and environmental circumstances. Critically ill patients, and specifically mechanically ventilated patients, exhibit severe sleep disruption patterns. Some factors predisposing to sleep disturbances are non-modifiable (age, cerebrovascular disease, but others can be improved (noise, excessive light, sedatives, hypotension). Studies on sleep in ICU patients are scarce due to the cumbersome and technical difficulties of polysomnographic tests. The recent validation of automated sleep studies are a promising field of research.

Delirium is an acute mental disturbance characterized by confused thinking and disrupted attention usually accompanied by disordered speech and hallucinations. Hospitalized, and mostly ICU, patients develop delirium at a variable incidence between 5% and 40% depending on case-mix and individual predisposing factors. Development of delirium during hospitalization is associated with higher mortality and long-term neuropsychological sequela. Because treatment of delirium is very poor, the research agenda is mostly focused in delirium prevention.

The role of mechanical ventilation (MV) on sleep disturbances is not fully understood, but international guidelines recently suggest the use of assist-control modes during sleep. In the MV field, patient-ventilator interaction has gained wide interest after the association of asynchronies with longer MV, weaning failure, and mortality. Nowadays, the availability of systems of continuous monitoring of ventilator waveforms allows the 24-h surveillance of asynchronies in MV patients.

Therefore, our hypothesis is that patient-ventilator asynchronies at night, but also during the day, may be associated with sleep disruption and the secondary development of delirium in critically ill patients.

Study design

This is a prospective observational cohort study involving 50 patients under mechanical ventilation in the Intensive Care Unit.

Study subjects and recruitment

Inclusion criteria:

- Age >18 yr.
- Patients who have survived the initial critical admission phase (severe hypoxemia or shock) and before approaching weaning.
- Consent to participate.

Exclusion Criteria:
- Presence of recent major central nervous system disease impairing consciousness with Glasgow Coma Scale ≤ 8T
- Patients with a sleep breathing disorder when it is predominantly central sleep apnea; patients with predominantly obstructive sleep apnea can be included.
- Severe hemodynamic instability (high dose of vasopressors).
- Receiving muscle paralysis.
- Withholding and/or withdrawal of life support treatments.

Patients will retain the possibility to abandon the study at any step without restrictions.

Data collection and management

After enrolment, every night, sleep architecture will be recorded using modified PSG (Prodigy. Cerebra-Health. Canada) (electroencephalography, right and left electrooculography, submental electromyography and electrocardiography) from 24:00 to 8:00. Pulse oximetry (SpO2) and heart rate will be recorded continuously during the PSG.

Mechanical ventilation will be continuously monitored by Better-Care system with specific algorithms for detection of asynchronies (ineffective efforts during expiration, double-cycling, short cycle, long-cycle, and asynchrony index), with additional capabilities (trapped gas, presence of secretions, pulse pressure variation,…).

Analgo-sedation will be administered as per local protocol. Dosage of continuous analgo-sedation will be recorded hourly by electronic surveillance. Level of sedation will be assessed by Ramsay score, whereas pain will be assessed by Campbell score or Visual Analog Scale when appropriate every 8 hours, or more frequently if deemed appropriate.

Delirium will be assessed by using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) every 8 hours (at 08:00, 16:00 and 24:00) from day 0 until discharge.

Sleep protective measures (earplugs, eye mask, avoidance of nocturnal feeding, light and noise reduction) will be routinely administered as per local protocol.

When feasible, sleep studies may be recorded in subsequent days to account for technical losses in the first study, and to get some insights about the trend in sleep disruption during ICU stay.

Outcome Measures

Primary Outcome Measures:

Correlation between sleep architecture (total sleep time, % of rapid eye movement sleep, sleep quantity (or efficiency), slow wave sleep and circadian sleep ratio, % of "pathological/atypical" sleep patterns, and sleep continuity) and asynchronies [Time Frame: 24 hours]

Secondary Outcome Measures:

1. Comparison of sleep disturbances between diurnal and nocturnal asynchronies [Time Frame: 24 hours]
2. Correlation between asynchronies and delirium [Time Frame: Up to 28 days]. Assessed using the Confusion Assessment Method for the Intensive Care Unit each day until ICU discharge.
3. Correlation between sleep disruption and delirium. [Time Frame: Up to 28 days]. Assessed using the Confusion Assessment Method for the Intensive Care Unit each day until ICU discharge.
4. Correlation between heart rate variability, asynchronies and sleep disturbances. [Time Frame: Up to 28 days].

Statistical plan

Sample size:
Based on the exploratory nature of the study, there is no strict sample size calculation, and higher sample size only will reduce the uncertainty of the estimation. Then, we decided a convenience sample of 50 patients.

Analysis:
Continuous variables will be described as mean and standard deviation when normally distributed and by median and interquartile range otherwise. Categorical variables will be described as frequency and percentages.

Continuous variables will be compared by ANOVA test when normally distributed and by Kruskall-Wallis test otherwise. Categorical variables will be compared by chi-square test.

The association of delirium with clinical variables will be analyzed by logistic multivariable regression analysis.

Trial organization

Acceptance by Ethics Committee: December 1, 2018
Actual Study Start Date: January 1, 2019
Actual Primary Completion Date: January 1, 2020

Ethical aspects

The study will follow the legal standards for clinical research in Spain. Specifically, the project needs the approval of the Ethics Committee of the "Unió Catalana d'Hospitals" and informed consent should be obtained from the patient's closest relatives.

The available evidence supports that patients will not be harmed in any way by the participation in this study. Then, no extra insurance coverage is needed.

Funding

This is an investigator-lead study without funding from external sources.

Sleep studies materials will be supplied by CerebraHealth free of charge as a research agreement with Althaia Xarxa Assistencial Universitaria de Manresa.

Asynchronies monitoring is already part of the routine ICU monitoring after an agreement between BetterCare and Althaia Xarxa Assistencial Universitaria de Manresa.

Experience of the investigator team

The investigator team has a wide experience in clinical and physiologic studies in critically ill patients, frequently supported by grants from public agencies.

Both collaborators (CerebraHealth and BetterCare) also have extensive experience in research projects.

Strategic Framework and Applicability of the results

The study is framed in a vibrant field of research, the interplay between mechanical ventilation and sleep either as co-factors or cause-and-effect, with delirium as the most important patient-oriented outcome.

The results of the study, if positive, may have direct application in a wide population of critically ill patients in any ICU.

References

1. Drouot X, Cabello B, d'Ortho MP, Brochard L. Sleep in the intensive care unit. Sleep Med Rev. 2008 Oct; 12(5):391-403. http://dx.doi.org/10.1016/j.smrv.2007.11.004 . Review.

2. Roche Campo F, Drouot X, Thille AW, Galia F, Cabello B, d'Ortho MP, Brochard L. Poor sleep quality is associated with late noninvasive ventilation failure in patients with acute hypercapnic respiratory failure. Crit Care Med. 2010; 38 (2):477-85. http://dx.doi.org/10.1097/CCM.0b013e3181bc8243

3. Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: Current and future trends. Respir Care 2018, 63 (4): 464-478 http://dx.doi.org/10.4187/respcare.05949 PMID: 29487094

4. Blanch Ll, Villagra A, Sales B, Montanya J, Lucangelo U, Lujan M, Garcia-Esquirol O, Chacon E, Estruga A, Oliva JC, Hernandez-Abadia A, Albaiceta GM, Fernandez-Mondejar E, Fernandez R, Lopez-Aguilar J, Villar J, Murias G, Kacmarek RM. Asynchronies during mechanical ventilation are associated with mortality. Intensive Care Med 2015; 41: 633-641. http://dx.doi.org/10.1007/s00134-015-3692-6 PMID: 25693449.

5. Younes M, Soiferman M, Thompson W, Giannouli E. Performance of a New Portable Wireless Sleep Monitor. J Clin Sleep Med. 2017 Feb 15;13(2):245-258. PMID: 27784419 http://dx.doi.org/10.5664/jcsm.6456

6. Younes M, Younes M, Giannouli E. Accuracy of automatic polysomnography scoring using frontal electrodes. J Clin Sleep Med. 2015;12(5):735–746. http://dx.doi.org/10.5664/jcsm.5808 PMID: 26951417

7. Younes M, Ostrowski M, Soiferman M, Younes H, Younes M, Raneri J, Hanly P. Odds ratio product of sleep EEG as a continuous measure of sleep state. Sleep. 2015 Apr 1;38(4):641-54. http://dx.doi.org/10.5665/sleep.4588 PMID: 25348125

8. Stein PK, Pu Y. Heart rate variability, sleep and sleep disorders. Sleep Med Rev. 2012 Feb;16(1):47-66. http://dx.doi.org/10.1016/j.smrv.2011.02.005 PMID: 21658979

Appendix 1. CRF of the study

Relationship between Asynchronies and Sleep Disruption in Mechanically Ventilated Patients: a prospective cohort study.

CHECKLIST FOR ENROLLMENT

BetterCare software OK: [ ] YES   [ ] NO

Prodigy available: [ ] YES   [ ] NO

Informed Consent obtained: [ ] YES   [ ] NO

Study Number: _ _

ICU Admission: Date _ _ / _ _ / _ _ _ _   Hour: _ _ / _ _

Age: _ _ years

Sex: Male [ ]   Female [ ]

Weight: _ _ _ kg

Height: _ _ _ cm

COMORBIDITIES:
HEART FAILURE   YES [ ]   NO [ ]
NEUROMUSCULAR DISEASE   YES [ ]   NO [ ]
COPD   YES [ ]   NO [ ]
DIABETES   YES [ ]   NO [ ]
CANCER   YES [ ]   NO [ ]
RENAL FAILURE   YES [ ]   NO [ ]
LIVER CIRRHOSIS   YES [ ]   NO [ ]

ADMISSION DIAGNOSIS: _____

APACHE II ON ADMISSION: _ _ (sum up the worse values within 24 h of admission)

PUNTAJE	4	3	2	1	0	1	2	3	4
temp.	≥41	39-40.9		38.5-38.9	**36-38.4**	34-35.9	32-33.9	30-31.9	≤29.9
PAM	≥160	130-159	110-129		**70-109**		50-69		≤49
frec. card.	≥180	140-179	110-139		**70-109**		55-69	40-54	≤39
frec. resp.	≥50	35-49		25-34	**12-24**	10-11	6-9		≤5
Pa/FiO2	<75	76-150	150-200	200-300	>300				
PaO2 (O2<.5)					**≥70**	61-70		55-60	≤55
pH arterial	≥7.7	7.6-7.69		7.5-7.59	**7.33-7.49**		7.25-7.32	7.15-7.24	≤7.15
sodio	≥180	160-179	155-159	150-154	**130-149**		120-129	111-119	≤110
potasio	≥7	6-6.9		5.5-5.9	**3.5-5.4**	3-3.4	2.5-2.9		<2.5
Creat (IRAx2)	≥3.5	2-3.4	1.5-1.9		**0.6-1.4**		<0.6		
hematocrito	≥60		50-59.9	46-49.9	**30-45.9**		20-29.9		<20
RB (miles)	≥40		20-39.9	15-19.9	**3-14.9**		1-2.9		<1
puntaje SNC (puntaje=15-Glasgow)							15 - .... =		

DAY OF THE STUDY

Data: _ _ / _ _ / _ _ _ _

FiO2: ____   VT: ____ ml   Mode: _____   PEEP: ____   PeakPaw: ____

Resp Rate: ____

SpO2: _____

Heart rate: _____

Systolic blood pressure: _____   Diastolic blood pressure: _____

Continuous sedatives: NO [ ]   YES [ ] Daily dose: _____

Continuous opioids: NO [ ]   YES [ ] Daily dose: _____

Ramsay: 0-8 h: ____   8-16 h: ____   16-24 h: ____

Campbell [ ] VAS [ ]   0-8 h: ____   8-16 h: ____   16-24 h: ____

CAM-ICU: 0-8 h: ____   8-16 h: ____   16-24 h: ____

NIGHT SURVEILLANCE

Light reduction: YES [ ]   NO [ ] Reason: _____

Noise reduction: YES [ ]   NO [ ] Reason: _____

Critical incident: NO [ ]   YES [ ] Describe: _____

Extra-sedation: NO [ ]   YES [ ] Describe: _____

SOFA Assessment (only during ICU stay)

	Days after enrollment										
	0	1	2	3	4	5	6	7	14	21	28
Respiratory											
Coagulation											
Liver											
Cardiovasc.											
CNS											
Renal											
Total											

Puntuación SOFA

	0	1	2	3	4
Respiratorio: Po2/Fio2	> 400	≤ 400	≤ 300	≤ 200*	≤ 100*
Renal: Creatinina/Diuresis	< 1,2	1,2 - 1,9	2,0 - 3,4	3,5 – 4,9 < 500 ml/día	≥ 5 < 200 ml/día
Hepático: Bilirrubina	< 1,2	1,2 – 1,9	2,0 – 5,9	6,0 - 11,9	≥ 12
Cardiovascular PAM o Fármacos	No hipotensión	PAM < 70	Dopa ≤ 5 ó Dobutamina	Dopa > 5 ó NA ≤ 0,1	Dopa > 15 ó NA > 0.1
Hematológico: Plaquetas	> 150.000	≤ 150.000	≤ 100.000	≤ 50.000	≤ 20.000
Neurológico: GCS	15	13 - 14	10 - 12	6 - 9	< 6

Respiratorio: pO2/FiO2 en mmHg. Puntos 3-4 solo se valoran si precisa ventilación mecánica.
Renal: Creatinina en mg/dl. Puntos 3-4 en caso de fracaso renal funcional u oligoanuria.
Hepático: Bilirrubina en mg/dl.
Cardiovascular: PAM (presión arterial media) en mmHg. Fármacos vasoactivos administrados durante más de 1 hora. Dopa = Dopamina. NA = Noradrenaliona o Adrenalina (dosis en mcg/kg/min).
Neurológico: GCS = Glasgow Coma Score

OUTCOME:

DELIRIUM: [ ] NO

                [ ] YES   Start: _ _ / _ _ / _ _ _ _   Hour: _ _:_ _

                                       End: _ _ / _ _ / _ _ _ _   Hour: _ _:_ _

WEANING FAILURE: [ ] NO   [ ] YES

TRACHEOSTOMY: [ ] NO   [ ] YES

ICU discharge (date):   _ _ / _ _ / _ _ _ _   ALIVE: YES [ ]   NO [ ]

Hospital discharge (date):   _ _ / _ _ / _ _ _ _   ALIVE: YES [ ]   NO [ ]

Appendix 2. Logbook for confidential identification of enrolled patients.

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REGISTRY OF ENROLLED PATIENTS (LOGBOOK)

(CONFIDENCIAL AT ENROLLMENT CENTER)

Nº of study patient	Data	Family name/First name	Chart Number	
1	_ _/_ _/_ _			
2	_ _/_ _/_ _			
3	_ _/_ _/_ _			
4	_ _/_ _/_ _			
5	_ _/_ _/_ _			
6	_ _/_ _/_ _			
7	_ _/_ _/_ _			
8	_ _/_ _/_ _			
9	_ _/_ _/_ _			
10	_ _/_ _/_ _			
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36	_ _/_ _/_ _			
37	_ _/_ _/_ _			

38	_ _ / _ _ / _ _			
39	_ _ / _ _ / _ _			
40	_ _ / _ _ / _ _			
41	_ _ / _ _ / _ _			
42	_ _ / _ _ / _ _			
43	_ _ / _ _ / _ _			
44	_ _ / _ _ / _ _			
45	_ _ / _ _ / _ _			
46	_ _ / _ _ / _ _			
47	_ _ / _ _ / _ _			
48	_ _ / _ _ / _ _			
49	_ _ / _ _ / _ _			
50	_ _ / _ _ / _ _			

Appendix 3. Eligible patients not enrolled in the study.

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PATIENTS NOT ENROLLED

Identification	Data	Exclusion criteria					Consent refusal	Without exclusion criteria			
		Neurological disease	Sleep disorder	Hemodynamic instability	Muscle paralysis	Withholding/ withdrawal therapy		Researcher missing	Lack of sleep monitoring device	Medical decision	Other
1	_/_/_										
2	_/_/_										
3	_/_/_										
4	_/_/_										
5	_/_/_										
6	_/_/_										
7	_/_/_										
8	_/_/_										
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