RESPIRATORY DEPRESSION IN OPIOID DEPENDENT CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

[1]B Tas, [1,4]NJ Kalk, [2,5]PSP Cho, [3]M Lozano-Garcia, [2]GF Rafferty, [4]M Kelleher, [2]J Moxham, [1,4]J Strang, [5,6]CJ Jolley. *[1]National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience (IoPPN) at King's College London, London, UK; [2]Division of Asthma, Allergy and Lung Biology, King's College London, London, UK; [3]Biomedical Signal Processing and Interpretation group, Institute for Bioengineering of Catalonia (IBEC), Catalonia, Spain & Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBERBBN), Barcelona, Spain; [4]South London and Maudsley NHS Foundation Trust, London, UK; [5]Centre of Human and Aerospace Physiological Sciences, King's College London, London, UK; [6]King's College Hospital NHS Foundation Trust, King's Health Partners, London, UK*

Introduction In the UK, opioid-related deaths are at record numbers after continually increasing year-on-year (ONS, 2019). This increase is believed to be driven by an ageing cohort of people with Opioid Use Disorder (OUD) and a high prevalence of comorbidities including chronic obstructive pulmonary disease (COPD). Our previous findings suggest that the degree of acute opioid-induced respiratory depression is greatest in OUD patients with chronically-suppressed neural respiratory drive (NRD) as a consequence of drug misuse (Jolley et al.,2015). We investigated the severity of respiratory depression in OUD and tested whether OUD exhibit more severe respiratory depression than matched controls.

Methods A convenience sample of opioid addicts receiving treatment at a community Drug & Alcohol Treatment Centre were recruited: OUD with normal lung function (OUD) and OUD with comorbid COPD (OUD-LD). OUD groups were matched with healthy controls (HC) and COPD patients with no history of drug/alcohol addiction (LD-Controls) from our laboratory database.

SpO_2%, end-tidal CO_2 ($ETCO_2$), transcutaneous CO_2 ($TcCO_2$), respiratory airflow and NRD index (NRDI), quantified using second intercostal space parasternal muscle electromyography (EMG_{para}), were measured continuously over 40mins at rest. Significant respiratory depression was defined as: SpO_2%<90% for >10s, $ETCO_2$ per breath >6.5kPa, $TcCO_2$ overall mean >6.5kPa, respiratory pauses (absence of inspiratory airflow) >10s.

Results Seven OUD patients (5M/2F, age: 48(46–52), FEV_1% pred(%): 96.1(90.5–96.5), FEV%FVC(%): 74.7(71.9–76.8)), 13 OUD-LD (11M/2F, age: 49(42–55), FEV_1%pred(%): 77.1 (66.8–90.1), FEV%FVC(%): 60.2(48.7–64.3)), 7 HC (6M/1F, age: 50(45–57), FEV_1%pred(%): 100(97.5–110.3), FEV%FVC (%): 75(69.7–78.5)) and 13 LD-Controls (10M/3F, age: 66 (62–72), FEV_1%pred(%): 60(52.8–74.5), FEV%FVC(%): 52 (45–57)) were studied. At least one of the respiratory depression indicators was detected in all 20 participants with OUD (Table1). Overall, there was a greater frequency of significant respiratory depression in both OUD groups compared to controls, most commonly $ETCO_2$>6.5kPa (p=0.021;Table1). NRDI was significantly higher in LD-Controls than OUD-LD (217(43.7–504.5) min^{-1} and 148.5 (35–172.6) min^{-1}, respectively (p<0.01)), but there was no significant difference between OUD and HC (87.6(51.7–115.3) min^{-1} and 76.9 (52.8–164.2) min^{-1}, respectively (p=0.7)).

Conclusions Respiratory depression is frequently present in OUD patients with comorbid COPD and significantly more severe than in opioid-naïve controls. Further studies are required to determine the association between respiratory depression and overdose risk.

Table 1 Presence of respiratory depression criteria in all participants with OUD and their corresponding control groups. Fisher's exact test was used to test for differences between criteria, both groups showed significant differences. OUD without LD and healthy controls p=0.021, and OUD-LD and LD-controls p=0.0001. [1]participants took OST medication on the day of testing. OUD: Opioid Use Disorder; LD: Lung Disease; SpO_2: pulse oximetry; $ETCO_2$: end-tidal CO_2; $TcCO_2$: transcutaneous CO_2.

Number	SpO_2 <90% >10s	$ETCO_2$ breaths >6.6kPa	$TcCO_2$ >6kPa mean	Resp Pauses >10s	Number	SpO_2 <90% >10s	$ETCO_2$ breaths >6.6kPa	$TcCO_2$ >6kPa mean	Resp Pauses >10s
OUD without LD:					**Healthy controls:**				
1		✓		✓	1		✓		
2[1]		✓	✓	✓	2		✓		
5	✓			✓	3				
8			✓	✓	4				
9		✓	✓		5				
16		✓			6				
18[1]		✓		✓	7				
OUD-LD:					**LD-controls:**				
3[1]			✓		1				
4[1]		✓			2				
6[1]	✓	✓		✓	3				
7[1]			✓		4				
10[1]	✓		✓		5				
11	✓	✓		✓	6				
12		✓			7				
13		✓			8				
14	✓	✓	✓	✓	9		✓		
15[1]				✓	10		✓		
17		✓	✓	✓	11				
19		✓		✓	12				
20		✓			13				