**COVID -19 and Psychosocial effects of salbutamol MDI on Respiratory ventilation**

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**Abstract**

During2021year ,the COVID-19 has been highly psychosocial phenomena and will be diagnosis as crucial of the human race and his style life through physiological and biochemical actions in human history due to international development at this time for epidemic and pandemic corona patient who tend to be afraid should be infected the virus and lead to feeling of stress with fear and depression of the health problem has been highly importance for combating as “coronavirus info endemic diseases”.**The aim** of this study to investigation the risk management that included not just the threat itself but also how corona patient perceive and respond to the threat in Kirkuk city .**Methods**:The study done period for 8 weeks during2021 onset of march until mayo and patient need to be intensive care unit (ICU) due to acute respiratory syndrome (ARDS) with case induced mechanical respiration during regarding of respiratory capacity within indicated(tidal volume with positive end expiratory pressure PEEP and peak airway meter for plateau pressure within residual volume(RV) measurement and respiratory system compliance for detected PBW-index value and breathing rate during measuring(tidal volume X respiratory rate X Paco2) / (PBW X100 X37.5) and gas exchanges severe COVID‑19 ARDS patients for [1–10] day after hospitals in Kirkuk city have been turning for using more salbutamol MDI. **Result**: thirty one moderate and 19 severe ARDS COVID‑19 patients were studied after initiation of high PEEP protective ventilation for observed moderate decreasing respiratory system compliance 29.5 [23.1–40.4] mL/cmH2O at ending expiratory lung volume: 1100 [1611–1323] ml. Gas exchanges was hypercapnia 66 [55–72] mmHg during high physiological dead‑space (VD/VT) : 85 [79–95.5] % when ventilator ratio (VR): 2.7 [2.4–4.6]. VD/VT and VR was significantly decreased by inhaler(MDI) using. **Conclusion:** The early observation the course of COVID‑19 ARDS has been highly ventilation/perfusion mismatch when association with stress marker such as Psychosocial effects, therefore could be explained the highly PEEP setting after using instruments dead space which is salbutamol MDI.

**Key wards:COVID-19, Gas exchange, lung volume, salbutamol MDI.**

**Introduction**

**The aim** of the study to compartment the gas exchange mechanism by using salbutamol MDI for conservative Oxygen conception in patient with moderate to severe ARDS of COVID-19 and the influencing of high FiO2during ventilation to evaluate the reabsorption at election on lung stress under Psychosocial effects on gas exchange . The most important conduction to discuss the gas exchange in COVID-19 when increasing the breathing rate divers of dyspnea than hypoxia on the stressful managements **1**.This clinical process lead to physical loads of respiratory tidal capacity by parenchymal defecting and pleural diseases with skeletal muscle defect in the respiratory ducts during bronchospasam and cramping released for becoming stenosis, so the needed to requirement minute ventilation and summative mechanical work in breathing under patient not be marked dyspnea and low oxygen saturation lead to increase minute ventilation and highly exhaled the CO2 up to 50% from maximal voluntary ventilation **2**; therefore obese patients have bed and fall back breathing during respiratory distress syndrome and requiring to the( intensive critical care) ICU **3**. In adult population with COVID-19 transmission by inhaled virus within the air particularly in congestion of population and beggarly ventilation during settings; therefore **4**, the most scientific evidence does not indicate that transmission of COVID-19 occurring due to heating ventilation with air condition (HVAC) systems in same time when viral RNA has been detected within the air during the viability of virus infection for air circulated by HVAC system which has not been suggested, but COVID-19 is primarily transmitted by direct contact of droplets motivated from various infections, such as Screening and self-isolation of infected population **5**; Hygiene measuring and hand hygiene measuring during coughing with sneezing quarterly **6**;therefore respiratory source must be controlling by cleaning the environmental air for prevented the infection are mainly by reduce pathological risk factor because gas exchange occur by diffusion than depended on some factors ;such as body size or surface area and thickness of membrane within the level of the gases that is important to control this factors in COVID-19 7,**8**.

**1- Causes poor gas exchange in the lung**

 In physically the lung volume determining by the elastic forces of the lung parenchyma for surrounding tissue of alveolar surface tension for respiratory muscle strength with lung reflexes of air ducts **9**.The lung volume blowing in must pathological future such as airway obstruction and compression with obesity for scoliosis lead to restrictive diseases during pulmonary fibrosis with interstitial lung disease , tuberculosis within sarcoidosis and pleural effusion during rib injury which is diaphragm paralysis for heart failure among most people**10** .The physical loading on the respiratory system responsibly for high work of breathing during disease statesmen and depending on four factors; firstly is the elastic loads disruption tidal ,while the secondly is resistive loading on airflow such as bronchospasm for airway secretions with stenosis and the thirdly is inertial mass of the respiratory system such as an obese body habitus during the expanded ,so the most important factor that is minute ventilation requirement; therefore the minute ventilation mainly needed to work of breathing due to the doubling of minute ventilation doubles with other summative mechanical workload on the respiratory system **11**.

**2- COVID-19 defects during acute respiratory infections.**

 Coronavirus disease 2019 (COVID-19) is an acute respiratory defect resulting from severe acute respiratory syndrome coronavirus 2 which is SARS-CoV-2, during May 2020 for the Epidemic has about 3.5 million infection more than 238,000 deaths**12** .Although 85% of people with COVID-19 have acute respiratory infection ,so the mortality range from 2% to 7% Patients with COVID-19 pneumonia may occur because of hypoxemic respiratory failure**13**. Most patient with COVID-19 have highly ventilation rate and the risk factor may be result from increasing the dead space at ventilation and increased CO2 released from the inflammatory response; therefore most highly minute ventilation up to 60% of the 25 second and maximal voluntary ventilation about 75 L in one minute in young and adult patient when the tidal volume about of 1.9 L during the ventilation rate of 48 bpm in some cases ,such as asymptomatic hypoxia lead to absence of population dyspnea when the despite high minute ventilation could not be become **14** .

**3-Obesity and COVID-19**

In obese patient, the central mass of the respiratory system is increased and this effect is most be risk factor when patient is supine with shakedown and massed together with high minute ventilation; therefore the loading diagnosed by obesity may be raised during the work of breathing for adequate to cause symptom **15**. So , the obesity appears to be an important risk factor for COVID-19 clinical defect and poor proceed from it **16**, COVID-19 have systemic hypertension in obese patients and avoidance of systemic vasodilators during calcium channel blocker should be preserved HPV 17, so the researching the clinical physiology of COVID-19 pneumonia must be including right heart catheterization and echocardiography then the impaired human papillomavirus (HPV) phenotype which was confirmed with several drug for reducing HPV with might future, and some researching including the administration of almitrine which lead to increase the HPV and activated the carotid body for inhibition the endogenous vasodilator pathways 18, such as the cyclooxygenase pathway and the nitric oxide synthase pathway during methyl arginine analogs **19**. The range of enhancing(human papillomavirus) HPV has been with single lung anesthesia and then relies on HPV for created the dry operative field for lung with almitrine lead to increased HPV due to improved systemic oxygenation ;therefore in sometime, almitrine can cause peripheral neuropathy by the ability to enhance HPV for augment carotid body function tduring the ability to be beneficial effect in COVID-19 pneumonia **20**. Each of these clinical test should be performed in the clinical trial approved of stander the test to be assessment of coronavirus disease 2019 knownCOVID-19 under the transcription reverse polymerase chain reaction (RT-PCR) testing**21**, so the Chest computed tomography (CT) was recommended for carnal the cases that complementary tool during dislocating of staging COVID-19 pneumonia**22**.More common CT finding of COVID-19 pneumonia included the multifocal and bilateral ground glass opacities (GGOs) which has been consolidating in the peripheral posterior at lowering the lobe of the lung**23** ,so the pleural thickening after pleural effusion and for pleural fonts are less common CT finding in most cases during the infection and CT finding will be mild and moderate or healing completely ;therefore, the severe cases may development acute respiratory distress syndrome and pulmonary fibrosis for leading to lung volume respectively losses**24**.

**4- COVID-19 transmission**

COVID-19 known as SARS‐CoV‐2 and novel coronavirus, which is COVID19 virus has diameter range about between 0.08 to 0.14 μm 25. Which was diagnosed by transmission could be highly droplet for airborne pathway should be go away between an aerosol and a droplet ;therefore the aerosols are liquid and solid particles perceived for the air and dust with pollen**26** ; therefore the aerosols can be result by speaking with coughing and sneezing should be produced droplets were sufficiently smaller must and still the air borne when some activity producing more droplets is smaller most time. While the normal breathing output a few droplets prolonged for 24 hours and the total droplet loading is must be considerabling**27**.

**5- Oxygen saturation in COVID-19**

The oxygen saturation (SaO2) and partial pressure of arterial oxygen(PaO2) has been an sigmoidal relationship known as the Oxygen Dissociation Curve**28** and an interesting feature of the curve was flattened as saturation rising above 97% and could be steeply falls off below 95%.O2 to estimation the PaO2 under standard physiologic condition **29**;therefore, the PaO2measurement requiring arterial blood gas sampling that is an invasive time would be consuming with logistically challenging and lead to the industry invented for noninvasive method of estimation functional oxygen saturation from arterial hemoglobin under using the pulse oximeter (SpO2)for measuring the inspired oxygen level (PaO) from the Oxygen Dissociation Curve and the latter could be very suggested for clinicians during such elevation in the ventilation should be rapidly reduced the CO2**30**. This reduction in CO2 shift the oxygen-hemoglobin dissociation curve to the left with lowering PaO2 making the oxygen more available for using by the body most time and this lowering in PaO2 was resulting from increased affinity of hemoglobin of oxygen 31, which has beneficial effect of oxygen uptake in the lung and some time reduced oxygen unloading at the tissue levels **32**,so the aSpO2 threshold of95%as significantly arise at 97% saturation ith the patient’sPaO2 is about 65mmHg during associated the threshold due to moderate hypoxemia and leading to the flawed assumption where critical respiratory impairment exist. Ninety percent (90%) saturation for corresponding to 60-65 mmHg for PaO2 just when the patient exhibiting the Mechanical ventilation should be following the ARDS (Acute respiratory distress syndrome)neither recommendation**33**;therefore the Tidal volumes of 5-8 mL/kg must be predicted body weight with the lung volumes when the pressure must be controlling during the face of refractory hypoxemia(PaO2/FIO2< 150);therefore the prone positioning must be the first recommended therapy when no evidence of human infection with SARS-CoV-2 **34** ,which is resulting from infection aerosol for distributed through the ventilation system and duct of HVAC system for counting the risk very lowly during HVAC systems and must be including air condition unit has been of droplet nuclei for spreading through HVAC system within building the boat for parking alone air condition unit under air is re circulated and flowed producing and air condition units may be facilitated with spread of droplet excreted by infected people for distance longer made and with indoor space of HVAC systems must be complementary role in the decreasing the transmission of indoor space due to increasing the rate of air change and decreasing recirculation of air and must be increasing the uses of outdoor airbecoming**35.**

**6-The Geometrical modifications of ventilation in COVID-19**

 The specific technically which is represented the physical planning of mechanical ventilation systems and needed to be learning by scientific evidence within technical models**36**, so the minimize of the risk factor of transmission must be needed to take account within the expected number of users and with these types of user for activation these user and the technical specifications must be standard the mechanical ventilation system for reduction the risk of COVID-19 transmission in indoor spaces stilling and needed to be tuned the COVID-19 research developments**37**. The volumetric scenography will be need to defined the categories of room and location type for taking within account the room size, so the degree of enclosure and non-mechanical ventilation during the probable purpose for which the room will be used;**30** therefore ,the option must be provided for protection the building of subject to engineering modification along 24. In practically the expiratory volume recording by measuring forced vital capacity (FVC) and forced expiratory volume in one second (FEV)has not been suggested**38**. The blowing impedance barrier device does not have significant effect on FVC and FEV below at FEV 44mL) and peak expiratory flow (PEF -0.47 L·s); therefore, the significant differences between measurement the filters and without filters have been demonstrated for FVC and FEV of airway maybe resistance within specifically airway conductance (sGaw)**32**, these difference not doing needed to the average value of the measurement except for sGaw; therefore ,the line filter has been evidence that their filters does not altering stationer for the lung during measurement respectively (vital capacity and FVC with FEV1and PEF, mean forced expiratory flow between 28% and 85% of FVC and TLC within DL,CO**39**.

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**Patient & methods**

The study conducted a prospective physiological study in the ICU of corona virus center Bagdad Road and Review Board approved the protocol (committee’s reference number: 18/2021)when the patients’ next for kin signed informing for consent forms was a preliminary report of clinical trial40 . NCT number was NCT04486729,for sterilization the Metered-Dose inhaler MDI you must be used an aero chamber for reprocessing for utilizing the MDI used under non-immunosuppressed patient would be recycled the patient to discharged the dispensing an MDI of pharmacy member and will be heat sealing inhaler the Canister with a plastic actuator and cap at room each times41. When transfer all part of the inhaler and spacer for continued storage the patient and medication and Registered Nurse (RN) and Respiratory therapist (RT) and all pieces including drug canister with plastic actuator with cap the spacer for contained the patient of dispensing bag sent of the pharmacy and discard the patient label (by the plastic baggie)by the Shred-It bin for(RN) or (RT) treated with the content as bio hazardous for placing the bag in the designated bin each unit PPE team member and collecting MDIs from the bin with deliver the sterile processing of reprocess cleaning and disinfection the PPE team member should be wipe of bin the following and removed the items each day.42 All cases(50) cultures were taken of the MDI nozzle before and after infection with an alcohol prep pad acts after treatments were administered the Growth of Staphylococcus epidermis's in at least 5% of the cultures with all two types of specimens those taken after the nozzle and disinfected with an alcohol prep pad for other cases and the hospital assessed the failure for wiping the canister nozzle for an alcohol prep pad before patient using one of 18 (5.5%) cultures and resulting for the grow thing of Streptococci Group D which is Enterococci and the sterile processing department (SPD) personnel will be don the gloves for appropriate PPE of disinfecting the inhalers of the spacer for discarded the biohazard. canister of the drugs for plastic actuator with the mouthpiece and the cap should be wiped with 70% isopropyl alcohol for Removed the drug canister of the aplastic actuator for the Wipe each surfaces is interior or exterior with alcohol and Do not be submerge of the canister or nozzle in liquid that can be blocked the nozzle .for Ensure adequate dry time to allow as disinfection of Once dry and place the canister inside a new zip lock bag for sealed and Soaking the actuator for mouthpiece cap in Val sure® neutral the pH detergent the water for 10 min .must be the appropriate dilution rate is followed under Using a timer for Contact time of 10 min was vital for effective disinfection43. And Using the a nylon brush to scrub away for any visible in Once completed place the components of the HEPA dryer with cool for placing the a new zip-lock bag PHARMACY when the SPD will deliver the reprocessed the MDIs for Weigh canister and return to stock for inhalers under according to the table below the Place canister for actuator with mouthpiece for return to a separate inventory.44

**Procedure**

The patient was deeply sedated by protocol of fentanyl and paralyzed for the patient was ventilation at semi recumbent position of volume control mode when a tidal volume is 6mL/kg for prediction the body weight at square flow waveform is 0.3 seconds at the end inspiratory mechanism when respiratory rate between 17 - 33 breaths per minute for controlling the pH between 7.30 - 7.45, so the PEEP value is 8cmH2O randomly applied two different FiO2 for each patient and one strategy achievably liberal (99%) SpO2 for obtain a conservative (77 - 82%) SpO2 each period evaluated at the same day40. For using the software available each phase lasting 25 minute based on the study carried out 45 ; therefor ,they showed be about5 minutes which was enough time to achieve the stable PaO2level43. After the end of each period should be obtain the arterial with mixed venous blood samples for monitoring the respiratory system mechanics37, and should not be used a washout period between each phase for inspected related to the viability and safety of the patient and considering the critical status for each sample of the wide variety the factors that should be affected arterial oxygenation after mobilization the aspiration of secretion and position changing to extending the time of measurement should be led to limitation the intervention of longer period of the time that affected the standar care each unit of clinical state.46

**Statistical analysis**

Data were expressed as the mean ±standard deviation{SD}the number (percentage) was appropriate and the Shapiro ilk test used as normality test . Each sample Student`s t-test was using for assess the statistical significance difference between the two conditions of subjects and the data normally distributed at two-tailed p ≤ 0.05 was considering the statistically significant analysis and performed at R 4.0.3 {R Foundation for Statistical Computing at www.rproject.org} ..

**Result**

**Table 1 level of TLC& FVC in Covid-19 patient(n0=50)**

|  |  |
| --- | --- |
| **Ranged level of parameters** | **Parameters**(**no=50 patient**) |
| 48-63 | Age ranged years |
| 19-31 | Male- female |
| 27.6-31.1 | BMI kg/m2 |
| 160-380 | P/F(PaO2-FiO2 ranged liters) |
| 20-30 | Time in hospital(days) |
| 5-9 | Smoker(no) |
| 4male-6female | COPD(no) |
| 11 male-9 female | Asthma(no) |
| 85-93 | FVC(liters) |
| 82-89 | FEV-1 liters |
| 83/86 | FEV-1/FVC liters |
| 83 | TLC liters |
| 81 | RC/TLC liters |
| 7.44-7.42 | PH |
| 23.2-8.9 | DLCO liters |
| 75-98 | RV liters |

The cross sectional study underletting the physical examination for all corona patient and resting pulmonary function test(PFT) by Biomed in spirometer used for perform PFT which is TLC(83),FVC is(85-93liters),FVC-1 is(82-93liters) and DLCO(23.2-8.9liters),while the RV is(75-98liters) when the BMI is(27,6-31.1) for corona patients with single breath hold method according after 10 min resting ,when the mean of Partial pressure of oxygen is 98.4mmHg after walking for ten minute

**DISCUSSION**

The result showing the inhaler MDI should be considering the effectiveness of oxygenation indices could be implication not only in severity stratification of ARDS but also for the clinical decision making process47. The proper stabilization time and standardized ventilator settings have been showing the improved the severity stratification in classical ARDS for found that ,the selecting an FiO2of 0.5 achieving an SpO2 when not less than 88% allows to better identification patient for risk factor of death comparison within higher fraction of inspired oxygen for patient with highly percentage of shunt and low ventilation/perfusion (V/Q) value and increasing the oxygen supply significantly affected the gas exchange indices during the marginal effect on PaO2of higher concentrations perfused and ventilated alveoli that limited capacity to increase CaO2 by determination the PA-aO2 for Pa/AO2 that is expected considering theoretical PAO2could be rising same proportion the FiO2 when changed for provided the PaCO2 constant and PO2will not be deoxygenated blood by resulting low V/Q value will mixing with oxygenated blood coming from normal V/Q units and the patient which included in this study presented at 43% functional shunt average that explaining why each one in COVID-19 must be pathophysiological feature could be different from classical ARDS that application of highly oxygen concentrations affected of gas exchange showed be opposite effected and should be explained by three potential reason 48, Firstly one is the respiratory system mechanic during lung stress remaining unchanged after increasing FiO2 and indicate that the atelectasis formation was not significant limiting at the time of exposure by using of FiO2 lowering than 100% and Secondly is the impairment of the normal mechanism for hypoxemic vasoconstriction may be proposed as a possible causes to explaining the hypoxemia in COVID-19 to prevent the significantly alteration of respiratory mechanic when increasing FiO2should be not have the considerable effect for vasomotor tone 49, Third one is the adequate evaluation of shunt fraction that implied the application of FiO2 100% at condition was not accomplished50 .The lung volume was lowering generally for sever hypoxemia of corona patient that including the lowering the percentage predicted FVC and lowering FEV-1 with TLC and residual restrictive that impairment after 30 days for hospitalization discharged when the DLCO was more reducing(61.7-67.8 liters) and mean ranged of TLC is( 81.5-77.8) 51.

**Conclusions**: The using of maternal dose inhalers (MDI) lead to reduce the risk of respiratory syndrome through the COVID-19 infection could be decreased the availability for supply chain and Hospital needing to proactive start collecting after used MDI when sterilize the provided procedure for keeping the separated stock for case requiring for minimize the risk of contamination place for each institution that including Doctors or infection or SPD team and pharmacy to agree them from Psychosocial effects, so the gas exchange abnormalities during COVID-19 induced different form of acute respiratory distress syndrome(ARDS) and lung compliance lead to reduced lung volume and capacity after increasing the inflammatory markers when TLC reduced less than75.5% and DLCO was more reduced than61.23% predicted in severe hypoxemia corona patient and reduction the RV was found smaller than72% after30days hospitalization.

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