The Noninvasive Positive Airway Pressure Ventilation Therapy System: Modeling and MATLAB-based Investigating

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Abstract

Background: The noninvasive positive airway pressure ventilation (NPPV) has been widely applied in therapy for the respiratory patient in acute respiratory distress syndrome (ARDS) and chronic obstructive pulmonary disease (COPD), etc.

Objective: In order to help clinician to investigate the technologies and measures of NPPV, a therapy system model included the respirator, breathing circuit and patient was designed.

Methods: Consequently, the mathematical sub-models of respirator, breathing circuit and mask, and respiratory airway were developed. With these sub-models, the ventilation system model of NPPV was prepared. The MATLAB-Based simulation experimental platform of NPPV system was set up to conduct the simulation experiments. In addition, by using the active servo lung ASL5000, a physical experiment platform was designed for comparative tests. Both of simulated experiments and physical experiments were operated with the simulated patient in ARDS, COPD and patient without spontaneous breathing.

Results: The simulated experimental outputs are coincident with the physical experimental outputs ($P \geq 0.31$ with TTEST, $R \geq 0.92$ with CORREL).

Conclusions: The experimental results substantiated that the therapy system model of NPPV is operational and workable. With this system model, it will benefit clinicians and researchers to conveniently promote the development of NPPV.

Background

The respiratory diseases seriously threaten human health and life now. In the world, there are more than 3 millions of patients (more than 6% of the total deaths) a year die of the chronic obstructive pulmonary disease (COPD) alone^[1]. The common respiratory diseases mainly include COPD, acute respiratory distress syndrome (ARDS), respiratory failure, etc.^[2-4]. The therapies for patients in respiratory diseases are often assisted with the mechanical ventilation (MV). Since the infectious respiratory diseases appear, such as severe acute respiratory syndrome (SARS) and corona virus disease 2019 (COVID-19), the MV has been an important role in fighting against the pandemic and curing the infected patient^[5]. Now among the popular measures in MV, the noninvasive positive airway pressure ventilation (NPPV) is one of the most widely applied and effective ventilation^[6-7].

In order to reduce or avoid the risks of ventilation in clinical trials, throughout the years, many trials and observational studies were analyzed to determine what ventilator parameters would benefit or injury the respiratory patient^[8-9]. The virtual experimental ventilation is an operational measure for preclinical evaluation before the application of MV in patient. The development of ventilation system model of NPPV based on MATLAB is one of the most convenient and feasible measures. Usually, the respiratory airway model in resistance and compliance has been used to investigate the gas exchanging between the lung and atmosphere based on the electric circuit^[10-11]. But so far, there are few introduce about the

simulation therapy system model of NPPV which includes the sub-model of ventilation device (respirator) and the sub-model of respiratory patient.

Consequently, in the programming condition of MATLAB Simulink, a simulated experimental platform of NPPV was developed for conducting a serial of simulated ventilation experiments with the simulated respiratory patients in COPD, ARDS and patient without spontaneous breathing (SB). This developed system model of NPPV will conveniently promote developing the technologies in NPPV.

Results

After running simulation ventilation with a developed NPPV system therapy system more than 10 minutes, the results displayed in the simulation oscilloscope were collected as illustrated in Fig•1 (a), (b) and (c) which respectively demonstrate the experimental data curves for ventilating the patients in COPD, ARDS and patient without SB.

The simulated respiratory airflow (Qa_sim), pressure in lung (Pl_sim) and tidal volume (Vt_sim) were respectively compared with the actual respiratory airflow (Qa_act), pressure in lung (Pl_act) and tidal volume (Vt_act). As illustrated in Fig•2, here both of the simulation experimental output curves and the physical experimental output curves are coincident.

By using the TTEST algorithm and CORREL algorithm in EXCEL to analyze both groups of data collected in simulated experiments and physical experiments, the results of P and R were listed in Tab•1. $P \geq 0.31$ means the differences between both groups of data are not obvious. $R \geq 0.92$ means both are in good consistency.

Tab•1

the P-value and R-value between both groups of output data in simulated and physical experiments

Data Name	P-value with TTEST			R-value with CORREL		
	COPD	ARDS	Without SB	COPD	ARDS	Without SB
Respiratory flow	0.77	0.77	0.65	0.97	0.92	0.97
Pressure in lung	0.62	0.31	0.55	0.99	0.98	0.99
Tidal volume	0.78	0.92	0.75	0.99	0.97	0.99

Discussion

The simulation system model of NPPV is convenient and safe for researchers and clinicians to develop the technologies in NPPV. For example, more ventilation modes will be possibly proposed with setting hoped-for conditions and parameters in simulation experiments. With the simulation system model of NPPV, both of the respirator and respiratory patient can be simulated. Not only the ventilation conditions

but also the pathological features of the respiratory patient will conveniently be investigated. Additionally, if necessary in the next investigations, the sub-model of respiratory airway can be optimized with other model such as Resistance-Inertance-Compliance (RIC) model, augmented RIC model, etc ^[17].

One of the main purposes of NPPV is to promote the respiratory patient to inhale sufficient fresh air into the lung and exhale carbon dioxide (CO₂) out the lung thoroughly. The respiratory flow and tidal volume (V_t) are usually considerable indexes to decide the effective ventilation. The adequate V_t usually ranged in 8 ~ 10 mL•kg⁻¹ (or 400 ~ 800 mL) is one of the major prerequisites for normal breathing. Adequate leak volume also is an important prerequisite to avoid CO₂ retention happened in NPPV ^[18]. When the leak volume (V_{leak}) is less than the V_t, it is easy to cause that the CO₂ and other waste gases cannot be completely discharged, and can be inhaled again by patient. Therefore, the leak flow and leak volume were listed in the simulated experimental results for conveniently observing and determining the ventilation effect.

In NPPV, a high pressure and a large volume often possibly cause a pulmonary barotraumas such as tension pneumothorax, mediastinal emphysema, pulmonary emphysema, and so on. But a low pressure and a small volume often possibly cause the respiratory patient in defective ventilation ^[19]. Based on the simulation ventilation system model of NPPV mentioned in this paper, the respiratory mechanical parameters such as the volume of V_t and pressure of P_{lung} can be observed. Well investigations and observations though the simulated experiments operated in the system model will be beneficial to determine the setting of relevant NPPV parameters, and to reduce the possibility of injuries to patient.

Respiratory disease is one of the greatest threaten to human health and life safety. In present, one of most common therapy measures is to use NPPV with respiratory patient. Especially for the patient in severe acute respiratory syndromes (SARS), H7N9 avian influenza or Corona Virus Disease in 2019 (COVID-19), clinicians are more aware of the importance of treatment with NPPV ^[20]. The system model of NPPV developed in this paper includes the sub-model of respirator, the sub-model of breath circuit and nasal mask, and the sub-model of respiratory model. It is helpful for setting ventilation conditions and parameters to simulate the NPPV according to the pathological characteristics and symptoms appeared in different respiratory patients.

Conclusion

A simulation ventilation system model of NPPV including respirator, breathing circuit, oral-nasal mask and respiratory patient was developed based on MATLAB. The NPPV was carried out with the simulated patients in COPD and ARDS and patient without spontaneous breathing. By comparing the results from the simulated experiments and from the ASL5000-based physical experiments, the output data in both groups of experiments are consistent with the no obvious difference ($P \geq 0.31$) and high consistency ($R \geq 0.92$). And the experimental results illustrated that the developed simulation system model of NPPV is feasible to simulation ventilation with the respiratory patients. This system model of NPPV will be helpful

to reduce or avoid the risks of clinical trials, and to provide the premeditated measure for NPPV applied with the respiratory patient.

Methods

Modeling for Ventilation Therapy System

As shown in Fig•3, the ventilation therapy system of NPPV is composed of a NPPV respirator, a breathing circuit and a mask (oral-nasal mask/ or nasal mask, etc), and a respiratory patient. By using MATLAB version 9 (R2016a), the ventilation system model was designed with developing a sub-model of respirator, a sub-model of breaching circuit and mask, and a sub-model of respiratory airway.

The purpose of a NPPV respirator is to deliverer a positive pressure into the patient's airway to support his breathing. This pressure ensures that the patient's respiratory airway is unblocked. The airflow freely moves in the airway under the positive pressure. And then the gas is exchanged between the lung and the atmosphere. The common ventilation methods in NPPV respirator usually include pressure control ventilation (PCV) and (PSV). PCV/PSV is usually applied in the patients without/with spontaneous breathing.

As shown in Equ•1, it describes the output pressure of P_a from the respirator when the respirator is working in the PCV mode. In the period of inspiration ($T_I < t < T_E$), the pressure of P_a exponentially increases from the expired positive airway pressure (EPAP) to inspired positive airway pressure (IPAP). In the period of expiration ($T_E < t \leq T$), the pressure of P_a exponentially decreases from the IPAP to EPAP. Here τ_1 and τ_2 respectively expresses the time constant of rising and falling.

$$\begin{cases} P_a = (\text{IPAP} - \text{EPAP}) \times \left(1 - e^{-\frac{t}{\tau_1}} \right) + \text{EPAP} & (T_I < t < T_E) \\ P_a = (\text{IPAP} - \text{EPAP}) \times \left(e^{-\frac{t-T_E}{\tau_2}} \right) + \text{EPAP} & (T_E < t < T) \end{cases} \quad (1)$$

As shown in Equ•2, it describes the output pressure of P_a when the respirator is working in PCV mode. The respirator is triggered to output IPAP or EPAP at the time of T_{ltrig} or T_{Etrig} which deputy the start of inspiration or expiration. The ventilation cycle of T is the time span from current T_{ltrig} to next T_{ltrig} , or from current T_{Etrig} to next T_{Etrig} . In the period of inspiration or expiration, P_a exponentially increases from EPAP to IPAP or decreases from IPAP to EPAP.

$$\begin{cases} P_a = (\text{IPAP} - \text{EPAP}) \times \left(1 - e^{-\frac{t}{\tau_1}} \right) + \text{EPAP} & (T_{\text{Itrig}} < t \leq T_{\text{Etrig}}) \\ P_a = (\text{IPAP} - \text{EPAP}) \times \left(e^{-\frac{t - T_{\text{Etrig}}}{\tau_2}} \right) + \text{EPAP} & (T_{\text{Etrig}} < t \leq T) \end{cases} \quad (2)$$

With the NPPV, the airflow from the respirator is delivered to the patient's airway through the breathing circuit and mask. The airflow in the circuit and mask is described in the Equ•3. Where Q_m deputes the airflow provided by the respirator. Q_{leak} deputes the leak flow which flows to the atmosphere through the leak hole in the mask. Q_{in} and Q_{ex} respectively depute the inspiratory airflow and the expiratory airflow. During inspiration, the Q_m is separated into Q_{leak} and Q_{in} . During the patient's expiration, both of Q_m and Q_{ex} flow to the atmosphere as Q_{leak} . The leak flow of Q_{leak} is decided by the pressure of P_a in the mask as described in Equ•3. Where a, b are the coefficients of the exponential function.

$$\begin{cases} Q_m = Q_{\text{leak}} + Q_{\text{in}} & (T_I < t \leq T_E \quad \text{or} \quad T_{\text{Itrig}} < t \leq T_{\text{Etrig}}) \\ Q_{\text{leak}} = Q_m + Q_{\text{ex}} & (T_E < t \leq T \quad \text{or} \quad T_{\text{Etrig}} < t \leq T) \\ Q_{\text{leak}} = -a \times (P_a)^b \end{cases} \quad (3)$$

As shown in Fig•4(a), the human respiratory airway includes the respiratory track and the lung. The viscous resistance in the respiratory track and the pulmonary elastic force (or compliance) in the lung prevent the airflow moving. For easily understood, the viscous resistance in track (R_a) and the compliance in lung (C_L , reciprocal of the elastic force) are usually analogized as the equivalent electric resistance and the equivalent electric capacitance.

In Equ•4, it describes the pressure of P_a mathematically related to Q_a , R_a and C_L . Here R_a represents the viscous resistances in the respiratory track. C_L represents the compliance in the lung. Q_a represents the airflow in the airway. In the period of inspiration ($T_I < t \leq T_E$), $Q_a = Q_{\text{in}}$, and $R_a = R_{\text{in}}$, Q_{in} enters into the lung. In the period of expiration ($T_E < t \leq T$), $Q_a = Q_{\text{ex}}$, and $R_a = R_{\text{ex}}$, Q_{ex} exits from the lung.

$$\begin{cases} P_a = R_a \times Q_a + \frac{1}{C_L} \int_0^T (Q_a) dt \\ R_a = \begin{cases} R_{in} & (T_I < t < T_E) \\ R_{ex} & (T_E < t < T) \end{cases} \\ Q_a = \begin{cases} Q_{in} & (T_I < t < T_{EI}) \\ Q_{ex} & (T_E < t < T) \end{cases} \end{cases} \quad (4)$$

In the period of inspiration, the contracted respiratory muscles and the expanded chest cavity result a negative pressure in the lung, and the spontaneous inspiratory flow is inhaled into the lung. In the period of expiration, the relaxed respiratory muscles and the recovered chest cavity result a positive pressure in the lung, and the spontaneous expiratory flow is exhaled out of the lung. In Equ•5, it expresses the inspiratory effort pressure of P_m produced by respiratory muscle working^[12-13]. In Fig.4(b), the P_m is a mathematic function of time (t) which ranges in a respiratory cycle ($0 < t \leq T$). P_m is in decreasing ($0 < t \leq T_{pm_rise}$), holding ($T_{pm_rise} < t \leq T_{pm_hold}$), releasing ($T_{pm_hold} < t \leq T_{pm_release}$), and zero ($T_{pm_release} < t \leq T$).

$$P_m = \begin{cases} -P_{m_max} \times \sin\left(\frac{2\pi t}{4 \times T_{pm_rise}}\right) & (0 < t \leq T_{pm_rise}) \\ -P_{m_max} & (T_{pm_rise} < t \leq T_{pm_hold}) \\ -P_{m_max} \times \sin\left(\frac{\pi}{2} + \frac{2\pi(t - T_{pm_hold})}{4 \times (T_{pm_release} - T_{pm_hold})}\right) & (T_{pm_hold} < t \leq T_{pm_release}) \\ 0 & (T_{pm_release} < t \leq T) \end{cases} \quad (5)$$

Simulated Ventilation

As illustrated in Fig•5, with the programming environment in MATLAB simulink, a simulation experimental platform was designed. In this platform, the function module (FCN) of “Respirator” is designed to perform the function of Equ•1 and Equ•2. The time constants of τ_1 and τ_2 in Equ•1 and Equ•2 were taken as 0.1s and 0.05s respectively. The FCN of “Leakage” was designed to perform the function of Equ•3. The sub-model of respiratory track and lung was designed with an adjustable electric

resistance (R_a) and an adjustable capacitance (C_L) to perform the function of Equ•4. The FCN of “Spontaneous Breathing” was designed to perform the function of Equ•5.

The parameters in the respirator mainly includes IPAP, EPAP, breath rate (BPM), the ratio of inspiration time vs expiration time (IE), working mode (Mode) and the airflow of triggered threshold (Threshold). The respiratory parameters in the model of respiratory airway mainly includes inspiratory resistance (R_{in}), expiratory resistance (R_{ex}), lung compliance (CL), max inspiratory effort pressure (P_{m_max}), the ratio of inspiratory effort pressure in decreasing time (P_{m_riese}), holding time (P_{m_hold}) and releasing time ($P_{m_release}$). Secondly, the simulated experiments were carried to collect and observe the experimental results. In the virtual oscilloscope, the data curves were displayed.

PCV and PSV were designed in the model of NPPV respirator. “Mode = 0” means the PCV was set to support the breathing of the patient without spontaneous breathing. “Mode = 1” means the PSV was set for the patient in ARDS or COPD. In PSV, when the respiratory airflow proved by spontaneous breathing reaches the threshold, the respirator will be triggered to output IPAP or EPAP. The simulated breathing circuit meets the standard breathing circuit in size of $\varphi 2.2\text{ cm} \times L180\text{ cm}$. The simulated mask was designed to meet the oral-nasal mask (Bestfit-2M, curative Medical Inc, Santa Clara, CA). In Equ•4, the coefficients were set with $a \approx 0.2$ and $b \approx 0.65$. Setting the parameters of system model as shown in Tab•2^[14-16], the simulated respiratory patient in COPD or ARDS or without SB was proposed to be ventilated with the simulated respirator.

Tab•2

the set parameters in respirator and patients

Parameters		Respiratory patient		
		COPD	ARDS	Without SB
In respirator	IPAP/cmH ₂ O	20	12	15
	EPAP/cmH ₂ O	5	4	4
	BPM/b·min ⁻¹	-	-	15
	IE	-	-	0.67
	Model	PSV	PSV	PCV
	Threshold/L·min ⁻¹	2	2	0
In patient	Rin/cmH ₂ O·s·L ⁻¹	21	11	6
	Rex/cmH ₂ O·s·L ⁻¹	23	16	6
	C[mL·(cmH ₂ O) ⁻¹]	53	30	50
	Pm_max/cmH ₂ O·s·L ⁻¹	24	21	0
	bpm/b·min ⁻¹	18	25	0
	Pm_rise/%	35	27	0
	Pm_hold/%	0	0	0
	Pm_release/%	23	20	0
<p>Note: $T_{pm_rise} = Pm_rise\% \times T$, $T_{pm_hold} = (Pm_rise + Pm_hold)\% \times T$.</p> <p>$T_{pm_release} = (Pm_rise + Pm_hold + Pm_release)\% \times T$. $T = 60 \div bpm$ / or $60 \div BPM$, “-” means no used.</p>				

In order to prove the practicability of the simulation ventilation system of NPPV, one of best measures is to check the simulation results with physical experimental results. As shown in Fig•6, a physical experimental platform was designed with mainly using the active servo lung ASLI5000 (IngMar medical, USA) and the noninvasive respirator ST-30k (Hunan Micomme medical, China). The respirator of ST-30K was connected to the head model though a breathing circuit (d 2.2 cm×/180 cm) and a oral-nasal mask (Bestfit-2M). A simulated upper airway was inserted into the head model. And the upper airway was connected to the SL5000 though a breathing circuit (d 2.2 cm×/70 cm). On the base of physical experimental platform, also setting the same parameters as listed in Tab•1, a serial of physical experiments were conducted.

Abbreviations

NPPV: noninvasive positive airway pressure ventilation;	ARDS: acute respiratory distress syndrome;
COPD: chronic obstructive pulmonary disease;	SARS: severe acute respiratory syndrome;
COVID-19: corona virus disease 2019;	SB: spontaneous breathing;
MV: Mechanical ventilation;	Qa: respiratory flow;
Qleak: leak flow;	Pa: pressure in airway;
Plung: intrapulmonary pressure;	Pm: inspiratory effort pressure;
Vt: tidal volume;	Vleak: leak volume;
Qa_sim: simulated respiratory airflow;	PI_sim: simulated intrapulmonary pressure;
Vt_sim: simulated tidal volume;	Qa_act: actual respiratory airflow;
Vt_act: actual tidal volume;	PI_act: actual intrapulmonary pressure;
RIC: resistance-inertance-compliance;	PCV: pressure control ventilation;
PSV: pressure support ventilation;	EPAP: expired positive airway pressure;
IPAP: inspired positive airway pressure;	BPM: breath rate per minute;
IE: the ratio of inspiration time vs expiration time;	Rin: inspiratory resistance;
Rex: expiratory resistance;	CL: lung compliance;
Pm_max: max inspiratory effort pressure;	FCN: the function module.
Tpm_rise: the time of inspiratory effort pressure in decreasing;	
Tpm_hold: the time of inspiratory effort pressure in holding;	
Tpm_release: the time of inspiratory effort pressure in releasing;	
Pm_riese; the ratio of inspiratory effort pressure in decreasing time;	
Pm_hold: the ratio of inspiratory effort pressure in holding time;	
Pm_release: the ratio of inspiratory effort pressure in releasing time;	

Declarations

Availability of data and materials

Not applicable.

Competing interests

No potential conflict of interest was reported by the authors.

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Authors' contributions

YUAN YueYang wrote this paper. ZHOU Li review the English. XIE Lixin and HU Xingshuo checked the respiratory data.

LIU Wei prepared physical experiments. DAI Zheng prepared the NPPV respirator.

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Figures

Figure 1

the data curves of output in simulated experiments: respiratory flow (Q_a), leak flow (Q_{leak}), pressure in airway (P_a), intrapulmonary pressure (P_{lung}), inspiratory effort pressure (P_m), tidal volume (V_t) and leak volume (V_{leak})

Figure 2

the data collected in simulations compared to the data collected in physical experiments: simulated respiratory flow in simulation (Qa_sim), physical experimental respiratory flow (Qa_act), simulated intrapulmonary pressure (Pl_sim), physical experimental intrapulmonary pressure (Pl_act), simulated tidal volume (Vt_sim) and physical experimental tidal volume (Vt_act)

Figure 3
the diagram of ventilation system of NPPV

Figure 4
the model of respiratory and effort curve

Figure 6

the physical test platform