

# The “Warrior” system: a new useful emergency simulator to train clinical pharmacists in emergency medicine

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## Abstract

Clinical pharmacists are indispensable providers of emergency medical services. However, the training of Chinese clinical pharmacists in medical emergency skills is apparently insufficient.

The current study aimed to evaluate the effect of the “Warrior” emergency simulator application in the emergency medical education of clinical pharmacy students (CP students).

The “Warrior” system, which contains a pharmacokinetics/pharmacodynamics-linked model and a drug database, was successfully employed to train CP students and improve their capability to deal with various medical emergency situations. Both an objective (in-class) test and the subjective Dundee Ready Education Environment Measure (DREEM) were administered to 20 CP students, randomly divided into an intervention group and a control group, to estimate the teaching effect of the “Warrior” system.

The scores of CP students from the intervention group were significantly higher ( $P < .01$ ) in the in-class test than the scores of students from the control group due to the diverse situational teaching using the “Warrior” system. The results of the DREEM showed that CP students from the intervention group obtained considerably better ( $P < .01$ ) marks for “students’ perceptions of learning” and “students’ perceptions of atmosphere” than those from the control group. Furthermore, the intervention group scored much higher ( $P < .01$ ) than the control group on the total DREEM.

The “Warrior” system provides an excellent training path for clinical pharmacists that supplies a more realistic clinical simulation experience and significantly improves the teaching effect. The “Warrior” system exhibits high potential for future development in emergency medical education.

**Abbreviations:** PK = pharmacokinetics, PD = pharmacodynamics, DREEM = Dundee Ready Education Environment Measure, CP students = clinical pharmacy students.

**Keywords:** Clinical pharmacist, Dundee Ready Education Environment Measure, Emergency simulator system, pharmacokinetics/pharmacodynamics-linked model

## 1. Introduction

Clinical pharmacists are crucial providers of emergency medical services, who effectively support physicians’ medical activities.<sup>[1,2]</sup> The ability and competence of clinical pharmacists

directly and significantly impact the effectiveness of medical services.<sup>[3,4]</sup> The history of clinical pharmacy education, spanning 20 years, is very short compared to the overall history of pharmaceutical education in China. In traditional pharmaceutical education, the training of clinical pharmacy students (CP students) has been focused on the production, quality control, analysis, and testing of drugs. These rigid teaching ideas lead to an inflexible arrangement of courses. Thus, CP students are mainly taught common courses, including analytical chemistry, pharmaceutical engineering, and pharmacy. Additionally, there are almost no courses focusing on pathology, diagnostics, and other clinical subject areas included in clinical pharmacy education; thus, CP students learn little regarding physiology, which is a vital subject for emergency skill training. Moreover, the internship stage is mainly conducted in laboratories or pharmaceutical enterprises with very limited time spent in hospitals,<sup>[5]</sup> leading to insufficient development of student clinical knowledge and thinking. Although the education system has improved in recent years, the internship duration for CP students in hospitals is still short and includes few medical activities, which restricts the training of CP students’ clinical ability.<sup>[6]</sup>

An established emergency simulator system uses human body simulation technology to provide CP students with better clinical experience, especially with regard to urgent medical situations and emergency treatment. This emergency simulator system has been developed based on a human physiology engine called

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CH and Y-yW contributed equally to this work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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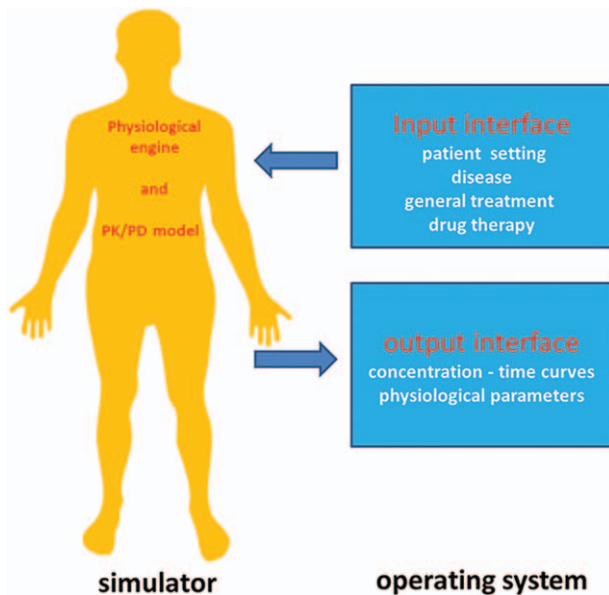
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**Figure 1.** Schematic representation and constituents of the “Warrior” system.

the “Warrior” system (Fig. 1). The program can configure personalized patient conditions and settings for diverse emergency situations. The “Warrior” system contains a larger drug database than other medical simulators and possesses a unique pharmacokinetics (PK)/ pharmacodynamics (PD)-linked model. The PK and PD drug activities in the “Warrior” system are calculated and holistically modified in real-time. CP students can estimate the correctness of their drug treatment decisions based on the PD performance. Furthermore, students can improve their results by modifying the treatment plan. Therefore, the “Warrior” system is more suitable for CP student education than other available systems.

In the current study, 20 students who studied in the same class were randomly split into 2 groups. Group 1 received traditional classroom instruction, whereas group 2 received emergency medical simulation training using the “Warrior” system. At the end of the course, objective (in-class) and subjective Dundee Ready Education Environment Measure (DREEM) tests were applied, to estimate the emergency response abilities of the 2 groups. The purpose of our study was to evaluate the effect of the “Warrior” system, which was used to train clinical pharmacist students in emergency medicine.

## 2. Methods

The study was approved by the ethics committee of Tianjin University of Traditional Chinese Medicine.

### 2.1. Simulator and settings

The simulated patient program in the “Warrior” system is based on a human physiology engine. Compared with other similar software programs, multi-system and multi-organ linkage has been successfully achieved in the “Warrior” system. Personalized virtual patients could be set by the teacher based on the teaching needs, and medical plans could be designed by CP students. The virtual patient received general treatment and drug usage commands from the CP students. With regard to the

drug treatment, students chose both the treatment drug and its dosage. The PK model, based on database-drug pharmacokinetic parameters, calculates drug plasma concentrations continuously and connects to the PD model through the plasma concentrations. The vital signs of the virtual patient were also displayed on a bedside monitor in real time. Students received feedback on the correctness of their drug and dosage regimen choices through vital sign changes of physiological parameters and the simulator.

In the input form, teachers could configure basic information (name, sex, age, height, weight, heart rate, respiratory rate, systolic pressure, diastolic pressure, and comorbidities) of virtual patients, disease settings (hemorrhagic disease, acute airway obstruction, or arrhythmia), and treatment options.

Furthermore, the “Warrior” system contains common emergency drugs, medical instruments (defibrillator, ventilator, and anesthesia machine), and common emergency treatment measures (hemostasis, infusion, blood transfusion, airway obstruction removal, asthma attack treatment, and tracheal intubation). A variety of therapeutic measures were available for students to choose and apply to virtual patients.

### 2.2. Drug methodology (database and PK/PD-linked model) of the “Warrior” system

The drug methodology of the “Warrior” system contains 2 models (a PK and a PD model) and a drug database including 50 medicines, their parameters (eg, logP, plasma protein binding rate, and degree of dissociation) derived from reputable database and literature sources such as DrugBank, PubChem, and PubMed. It involves commonly used emergency drugs, such as the cardiotoxic drugs digoxin, epinephrine, and dopamine; the airway dilation drug aminophylline; the respiratory stimulant nikethamide; capacity expansion drugs; the arrhythmia drugs lidocaine and amiodarone; and the painkillers morphine and pethidine, and so on.

The PK model describes the behavior of a substance or a drug from its entry into the body to its complete elimination, including its transport through the bloodstream, diffusion through the blood-tissue barrier, clearance, excretion, and metabolism. The “Warrior” program can simulate multiple drug delivery pathways, such as intravenous drip, intravenous or muscle push, and inhaled drug delivery. Moreover, the “Warrior” program mimics drug delivery in the body by moving substances with the blood flow, where drugs are transported to the intersection of capillaries and tissues. Diffusion is divided into perfusion-limited diffusion and osmotic-limited diffusion. The former depends on blood flow, drug concentration, and the distribution coefficient in tissue and plasma and is limited by the rate of blood flow to the organs; the latter is limited by the membrane permeability of each drug. The specific calculation method should be determined on the basis of the selected drug type and administration method.

The distribution coefficient represents the ability of an organ or tissue to absorb drugs, which is calculated based on the physical and chemical properties of drugs (Table 1). Formula (1) is used to determine the distribution coefficient of weakly alkaline, acidic, or neutral drugs. Formula (2) is utilized to obtain the distribution coefficient of strongly alkaline drugs. Formula (3) is used to calculate the mass of the drugs. The calculation of the drug-related organ allocation coefficient is shown in Figure 2.

**Table 1**

The PH effects on the partition coefficient are described based on the drug type, very weak base, acid, or neutral. X relates the drug property pKa to the pH of intracellular water, while Y relates the pKa to the pH of the plasma.

Ionic State	X	Y
Acid	$1+10^{(pH \text{ intracellular water} - pKa)}$	$1+10^{(pH \text{ plasma} - pKa)}$
Very weak base/base	$1+10^{(pKa - pH \text{ intracellular water})}$	$1+10^{(pKa - pH \text{ plasma})}$
Neutral	1.0	1.0

SD = standard deviation.

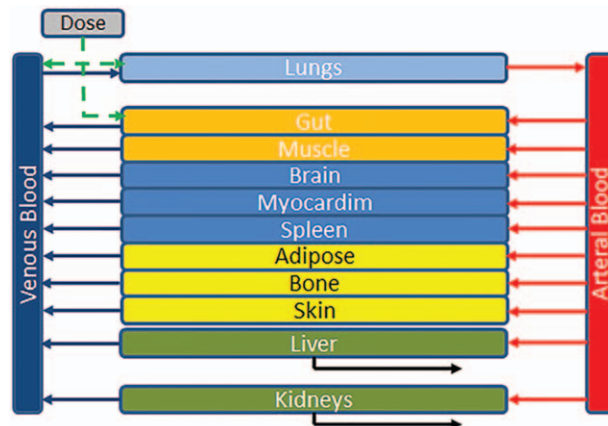
$$K_p = (X*f_{IL})/Y + f_{EL} + (P*f_{NL} + (0.3*P + 0.7)*f_{NP})/Y + \dots((1/R_b - 1 - (P*f_{NLP} + (0.3*P + 0.7)*f_{NPP})/Y)*P_T/P_B) \tag{1}$$

$$K_p = f_{EL} + (X/Y*f_{IL}) + (K_\alpha*AP_T*X)/Y + \dots(P*f_{NL} + (0.3*P + 0.7)*f_{NP})/Y \tag{2}$$

$$\Delta M_T = Q*dt*C_V - (Q*C_T)/K_p \tag{3}$$

Where X and Y are the different relationships for pH, as shown in Table 1, fIW is the fraction of intracellular water, fEW is the fraction of extracellular water, fNP is the fraction of neutral phospholipids in the tissue, fNL is the fraction of lipids in the tissue, P is the octanol water partition coefficient for the drug, fu is the fraction of unbound drug in plasma, fNL, P is the fraction of neutral lipids in plasma, fNP, P is the fraction of phospholipids in plasma, and PRT/PRB is the tissue to plasma ratio of the binding protein.

The PD model alters major physiological parameters, such as heart rate, diastolic and systolic blood pressure, respiratory rate, and bronchiectasis in accordance with the instantaneous plasma concentration of a drug. Such alterations are indicated by changes in the pharmacodynamic coefficient. For example, 0.5 represents 50% increase in the clinical effect indicated by the based value, whereas -0.2 represents 20% decrease.



**Figure 2.** The pharmacokinetic model represents substance transport throughout the cardiovascular system after dose administration, diffusion across the blood-tissue barrier, clearance, and substance metabolism.

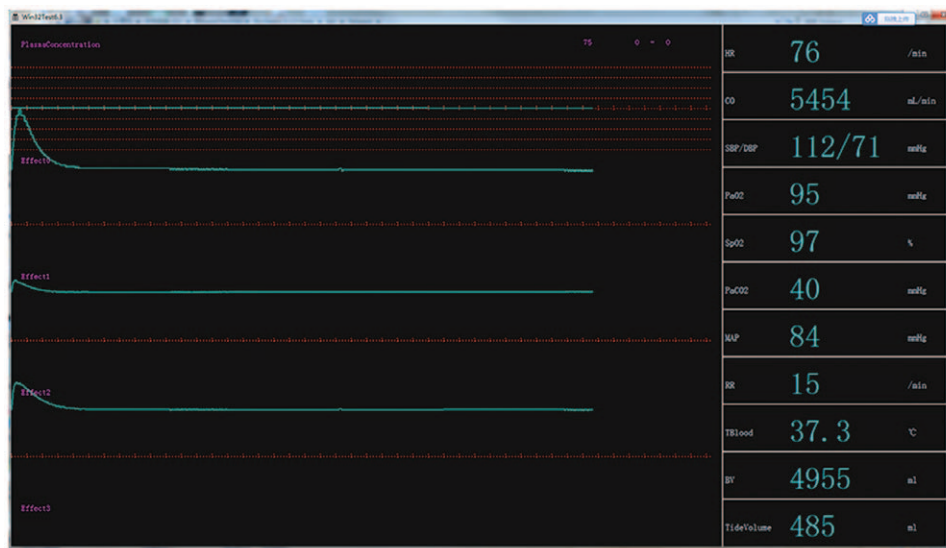
The 2 models are linked together by drug plasma concentrations and are presented in a PK/PD model (Fig. 3). Continuous changes of both efficacy (physiological parameters) and the time-concentration curve can be observed after administration.

**2.3. Training scenario settings**

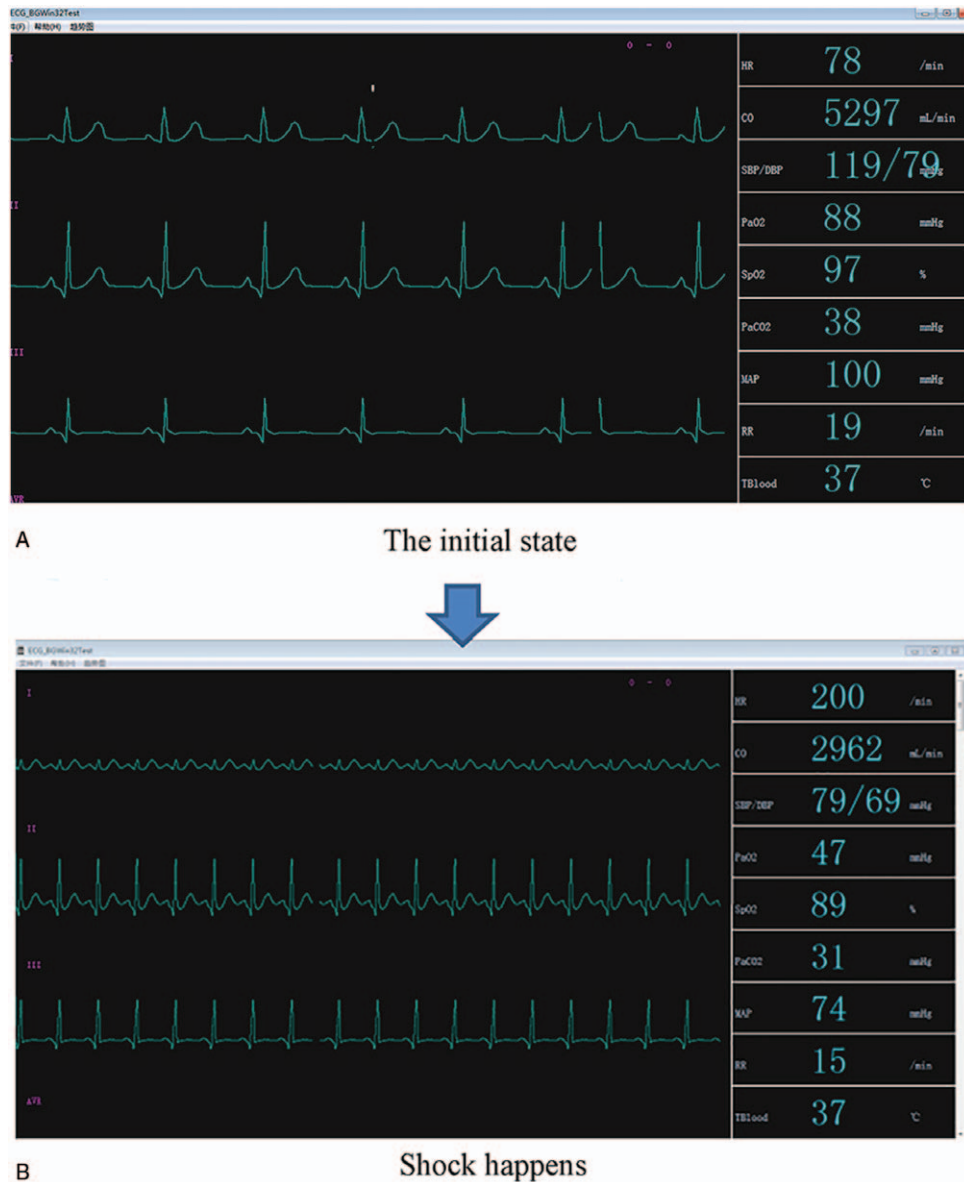
The “Warrior” system utilized several simulated emergency situations on a virtual adult male patient (40 years old, 180 cm tall, and weighing 70 kg) as described below.

**2.3.1. Simulated hemorrhage case.** In this case, a wound was present on the left leg of the virtual patient with 800 mL/min blood loss. The patient’s blood pressure decreased due to the bleeding, a series of symptoms appeared and progressed, and finally shock developed. The patient would have died in 5 minutes if no treatment was applied (Fig. 4).

Hemostatic therapy was administered, and the bleeding stopped. Then, 2000 mL whole blood and dopamine (5 µg/kg/min) were



**Figure 3.** Output interface of the PK/PD model, concentration-time curves, and physiological parameters. PK/PD = pharmacokinetics/pharmacodynamics.



**Figure 4.** Bleeding (A) The change of physiological status after setup left leg trauma of a virtual patient. A: Beginning of patient bleeding. B: The shock occurred as a result of blood loss.

infused intravenously, which normalized the patient's blood pressure. However, due to the excessive loss of blood oxygen, the patient's oxygen partial pressure remained very low, and type 1 respiratory failure developed. The respiratory rate dropped to 9 breaths/min. Simultaneously, with heart excitation, the heart rate increased to 200 beats/min. At this point, the patient would have died within 10 min, if the respiratory failure was not corrected (Fig. 5).

Nikethamide was infused, after which the lung's air exchange volume increased, the oxygen partial pressure recovered to more than 60 mm Hg, the respiratory and heart rates normalized, the respiratory failure was reversed, and tissue hypoxia was relieved (Fig. 6). Finally, the body returned to its original functional level after 10 min without any intervention (Fig. 7).

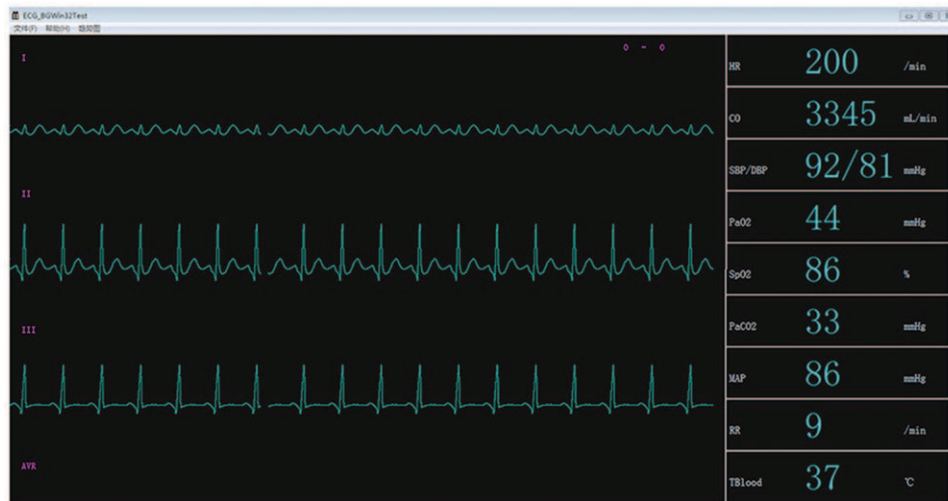
**2.3.2. Simulated arrhythmia case.** In this case, the patient developed ventricular tachycardia and his heart rate increased to

180–200 beats/min accompanied by abnormal wave shapes of the ECG. Next, 5 mg lidocaine was administered parenterally, after which the ECG and other diagnostic indicators normalized (Fig. 8).

**2.3.3. Simulated acute airway obstruction case.** The virtual patient experienced an asthma attack, his respiratory rate rose to 32 breaths/min, the oxygen partial pressure dropped to 58 mmHg, type 1 respiratory failure developed, and the heart rate increased to 111 beats/min. After 300 mg aminophylline intravenous drip, the respiratory rate and oxygen partial pressure of the patient returned to normal (Fig. 9).

#### 2.4. Participants

Twenty students attending the same class (10 male and 10 female) were randomly assigned to 2 groups, with an equal number of



**Type 1 respiratory failure happens**

**Figure 5.** Bleeding (B) Type 1 respiratory failure develops due to blood oxygen loss.

males and females in each group. There were no significant differences between the groups with regard to age, final score in the previous semester, intellectual development level, knowledge base, and learning ability (Table 2). The CP students from the control and intervention groups received normal instruction by teachers and training using the “Warrior” System, respectively.

**2.5. Tests**

The grades of both student groups had not differed significantly during the previous semester (Table 2). The control group received traditional classroom instruction, whereas the intervention group received emergency medical simulation training using the “Warrior” system. After the completion of the training, all CP students from both the control and intervention groups took the

same examination. The main topics of the in-class test included PD, clinical applications, and adverse reactions to emergency drugs in the database.

The DREEM questionnaire, used to subjectively test both groups in this study after the training completion, was developed by the Dundee University in 1994 and has been widely utilized in many countries around the world. The scale contains 50 items consisting of 5 dimensions,<sup>[7]</sup> namely, students’ perception of learning (12 items), students’ perception of teachers (11 items), students’ academic self-perception (8 items), students’ perception of the environment (12 items), and students’ self-social perception (7 items). Each item is graded on a scale of 5, from strongly agree (4 points) to strongly disagree (0 points), with a maximum score of 200 points.<sup>[8-10]</sup> The higher the score, the better the education effect.



**After respiratory stimulant treatment**

**Figure 6.** Bleeding (C) after respiratory stimulant treatment.



Figure 7. Bleeding (D) Physiological indicators return to normal with time.

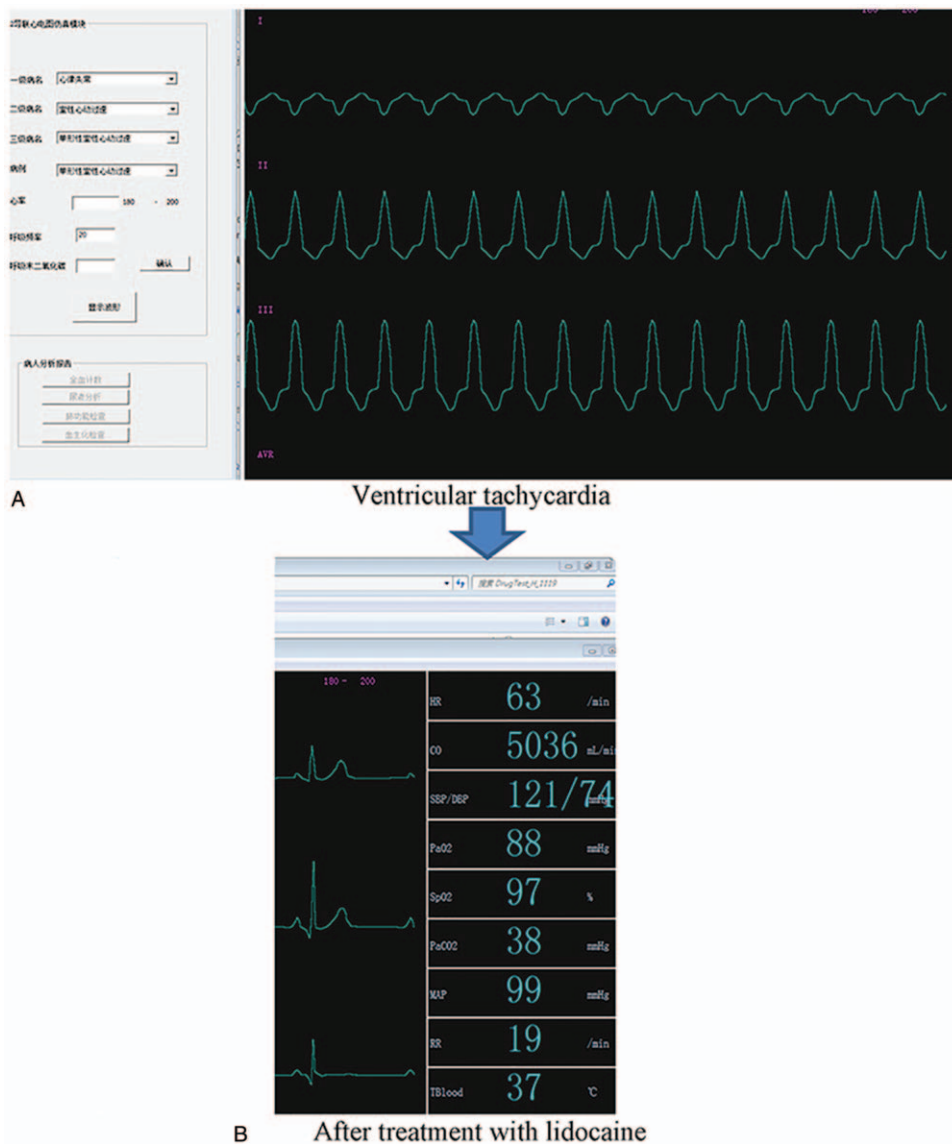


Figure 8. Arrhythmia A: Ventricular tachycardia. B: After treatment with lidocaine.



Figure 9. Acute airway obstruction A: Asthmatic attack B: Aminophylline treatment.

2.6. Analysis

The reliability of the DREEM questionnaire was measured using Cronbach’s alpha. SPSS version 19.0 was utilized for statistical analysis.

Table 3

DREEM scores for students of control group and intervention group (n=20) (Mean±SD).

Score allocated	Control mean ±SD	Intervention mean ±SD	P value
Students’ perceptions of learning	22.8 ±3.2	39.4 ±2.2*	<.001
Students’ perceptions of teachers	26.4 ±4.3	25.4 ±3.8	.61
Students’ academic self-perceptions	14.4 ±5.0	22.2 ±4.7	.03
Students’ perceptions of atmosphere	26.5 ±5.1	39.3 ±2.7*	<.001
Students’ social self-perceptions	16.3 ±4.1	17.1 ±2.9	.64
Total DREEM score	106.4 ±11.8	143.4 ±8.9*	.001

DREEM = Dundee Ready Education Environment Measure, SD = standard deviation. \* P < .01. versus control group.

Table 2

General information of students (n=20) (mean ±SD).

	Control (n=10) Mean ±SD	Intervention (n=10) Mean ±SD	P value
Age	21.2 ±0.6	21.3 ±0.8	.764
Score of Last semester specialized course	71.2 ±5.2	73.4 ±4.4	.344

SD = standard deviation.

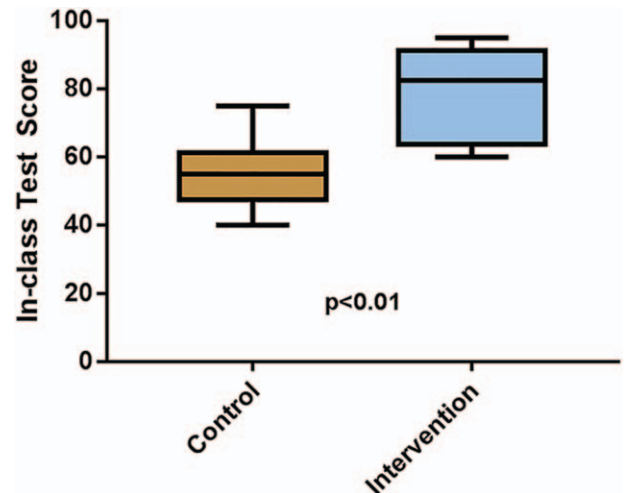


Figure 10. The in-class test score after emergency drug learning.

3. Results

3.1. Results of the in-class tes

The in-class test scores of the CP students in the intervention group (78±13.5) were significantly higher (P < .01) than those of the students in the control group (62±16.2) due to the situational teaching using the “Warrior” system Fig. 10. Thus, the application of the “Warrior” system improved students’ understanding and memorization of the study material; furthermore, it achieved better teaching results than the traditional classroom teaching mode.

3.2. DREEM questionnaire

Cronbach’s score was 0.829, indicating reliability. The scores of the intervention group for “students’ learning perceptions” and “students’ atmosphere perceptions” in the DREEM were significantly higher (P < .01) than the scores of the control group (Table 3). Furthermore, the intervention group achieved

considerably higher ( $P < .01$ ) total DREEM score than the control group. Students generally believed that the application of the “Warriors” helped them clarify their learning goals more efficiently than boring classroom teaching, provided a more vivid learning environment, and was closer to the clinical environment they would encounter after graduation.

#### 4. Discussion

The separation of the education system for clinical pharmacists from traditional pharmacology education in China has been relatively delayed. Moreover, there are many imperfections in the current education system for clinical pharmacists, especially the lack of clinical skills and clinical experience of new graduates. However, there is no difference between clinical pharmacists and clinicians with regard to the actual work,<sup>[4]</sup> and clinical pharmacists are required to have sufficient clinical experience to cope with various critical situations. Therefore, the potential lack of clinical experience will prevent them from using their professional skills and making correct decisions. We introduced medical simulators to enhance the training of clinical skills in CP students, which will help them correctly guide doctors in clinical use, especially in emergency situations.

At present, the most commonly used medical emergency simulators are SimMan and MUSE,<sup>[11,12]</sup> which have been designed primarily to educate doctors<sup>[12]</sup> rather than clinical pharmacists.<sup>[13]</sup> They contain many medical treatment options, such as intubation, hemostasis, piercing, and defibrillation. The content regarding treatment interventions is very rich, but the drug usage modules are markedly weak and few in number. Furthermore, programming in these systems is not based on a physiology engine and drug behavior is not based on a PK/PD model; thus, drug administration also does not conform to the actual situation and objective logic.<sup>[14]</sup>

Current medical emergency simulation programs are apparently far from meeting their teaching requirements.<sup>[15,16]</sup> Therefore, the “Warrior” System was developed, which presents 2 advantages. First, our “Warrior” system contains a larger database, including around 50 drug types for emergency medical simulation. Second, since the operation simulation of the “Warrior” system is based on a physical engine and PK/PD mode, drug behaviors are closer to the actual situation and objective logic. Simultaneously, there is a multiple organ system linkage and simulator performance is more consistent with the real performance of the human body, so that CP students receive a more realistic and profound learning experience.<sup>[17]</sup>

The positive effect of the “Warrior” system was also reflected in the student feedback. The in-class test score of the intervention group was obviously higher than that of the control group. The “Warrior system may significantly improve CP student perceptions of learning and of study atmosphere. Students prefer this teaching method, because it provides real-time feedback, is more vivid, and is closer to the real world than the traditional education approach. The “Warrior” system can greatly improve student education and mastery of knowledge and thinking; furthermore, it helps the students understand how to acquire knowledge in the study process and how to utilize in their work later.

#### 5. Conclusions

The implementation of the “Warrior” emergency treatment system was very successful. In the training of clinical pharmacists, it provides a rich and realistic clinical experience and improves

the teaching effect. The system development continues, since many modules are currently imperfect, including the endocrine and coagulation systems. Furthermore, drugs are presently administered via intravenous injections and intravenous drips, but oral drug systems will also be developed in the future. Moreover, the influence of drug interactions, which are important data for the work of clinical pharmacists, will be developed. Simultaneously, we will create more clinical cases and presentations, so that students can obtain greater clinical experience. Since the Warrior system has just begun to use, so the sample size was small, we will continue to promote it in the training of clinical pharmacists, we will do wider research, and provide research support to improve the improvement of the “Warrior” system. Briefly, the “Warrior” emergency simulator system provides a good training path for clinical pharmacists; some achievements have already been made, and the system will acquire more features in the future.

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**Visualization:** Jing-jie Zhou.

**Writing – original draft:** Cong Huang, Yang-yang Wang.

**Writing – review and editing:** Cong Huang, Jing-jie Zhou.

#### Corrections

Several corrections have been made to the author affiliations. Dr. Cong Hong was previous only affiliation a. Dr. Yang-yang Wang was previously affiliation b. Dr. Xin He was affiliation d. Affiliation d, School of Traditional Chinese Medicine, Guangdong Pharmaceutical University, Guangzhou, China, has been removed.

The corresponding author address has been changed from Tianjin University Traditional Chinese Medicine, Tianjin 301617, China, School of Traditional Chinese Medicine, Guangdong Pharmaceutical University, Panyu District, Guangzhou 510006, China.

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