



## Original Article

# Aerosol therapy during mechanical ventilation in intensive care units: A questionnaire-based survey of 2203 ICU medical staff in China<sup>☆</sup>



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## ABSTRACT

**Background:** To describe the current status of aerosol therapy during mechanical ventilation (MV) and the practice, knowledge, and beliefs about aerosol therapy in physicians working in the intensive care unit (ICU) in China.

**Methods:** A physician self-administered questionnaire-based cross-sectional survey was carried out from January 2019 to July 2019. An electronic questionnaire was designed, and physicians who worked regularly in ICUs across several hospitals were contacted through WeChat. Answers to all questions and the general characteristics of physicians who answered the questionnaire were collected and analyzed.

**Results:** A total of 2203 medical staff who regularly worked in the ICUs completed this questionnaire (9.0% missing data); 87.7% of the participants were doctors. Most respondents claimed that they often administered aerosolization therapy. Ultrasonic atomizer (50.7%) and jet nebulizer (48.6%) were the most commonly used atomization devices. Bronchodilators (65.8%) and steroids (66.3%) were the most frequently aerosolized drugs during MV. During nebulization, ventilator settings were never changed by 32.7% of respondents. Only 49.1% of respondents knew the appropriate place for a nebulizer. Further, 62.7% of respondents using heated humidifiers reported turning them off during nebulization. Specific knowledge about droplet size and nebulization yield was poor. Respondents from tertiary hospitals and those with higher technical title or work experience tended to have better accuracy than those from primary hospitals or with lower technical titles ( $P < 0.050$ ).

**Conclusions:** Aerosol therapy was commonly used during MV, and the most frequent drugs were bronchodilators and steroids. Scientific knowledge about the optimal implementation of aerosol therapy during MV seemed deficient.

## Introduction

Aerosol therapy, widely used for patients undergoing mechanical ventilation (MV), is a common practice in the intensive care unit (ICU). It is a method to deliver medicated particles by inhaled gases and is associated with improved long-term patient-centered outcomes.<sup>[1]</sup> More recently, inhaled antibiotics have been successfully used to treat tracheobronchial infections in outpatients with stable cystic fibrosis.<sup>[2]</sup> In the acute setting, particularly among critically ill patients under MV, aerosol ther-

apy is widely used to deal with various respiratory symptoms; however, the use of inhaled drugs, albeit appealing, is often hampered by the low amounts of drug available to the patient after inhalation.<sup>[3,4]</sup>

Subsequently, considerable research efforts have focused on understanding the factors affecting aerosol delivery during MV which are now relatively well described (ventilator setting, circuit setup, and humidification).<sup>[5–7]</sup> The efficiency of aerosol therapy was also promoted by the implementation of modern ventilators and aerosolization devices.<sup>[8,9]</sup> Physicians in the ICU

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play crucial roles in administering aerosol therapy, as their knowledge of aerosols can directly affect aerosolization efficiency.

Some studies have discussed the current practice of doctors administering aerosol therapy during invasive mechanical ventilation (IMV) and non-invasive mechanical ventilation (NIMV). In a previous study using an e-mail self-administered survey, the researchers obtained responses from 854 physicians who were confident in aerosol therapy efficacy and used it frequently for critically ill patients.<sup>[10]</sup> However, in their study, the clinicians' knowledge appeared to be very heterogeneous as the accuracy of specific knowledge was lower than expected.<sup>[10]</sup> A prospective cross-sectional point prevalence study in 81 ICUs across 22 countries in Europe also showed heterogeneous results in the implementation of aerosol therapy.<sup>[11]</sup>

China is a large country with substantial variances in the practice of aerosol therapy during MV.<sup>[12]</sup> Accordingly, sufficient information about the use of aerosol therapy by respiratory care practitioners and intensivists in China is lacking. Therefore, we designed this study to describe the current practice, knowledge, and opinions of ICU physicians in China regarding aerosol therapy during MV. We believe that this information will provide support for developing better policies and educational programs.

## Methods

### Study design

This physician, self-administered, questionnaire-based, cross-sectional survey was carried out from January 2019 to July 2019. Physicians from the comprehensive ICU, specific ICU, and pediatric ICU were included, and they participated by completing an online questionnaire. All physicians were given 30 min to complete this questionnaire, and we collected the data over eight periods during our conventional nationwide trainings of MV.

### Content of questionnaire

The questionnaire comprised 25 questions and was developed through question-item generation/reduction performed to fit the survey objectives and practicability.<sup>[13]</sup> This questionnaire included five aspects: (1) nebulizer therapy devices (jet, metered-dose inhalers, ultrasonic, and vibrating mesh nebulizers); (2) aerosolized drugs (bronchodilators, steroids, antibiotics); (3) ventilator and circuit (settings, device placement, humidification); (4) non-invasive ventilation (humidification, device placement); and (5) basic knowledge of aerosol therapy. There were four questions in the part on knowledge and beliefs:

- Q1. Do you agree that only small droplets reach the trachea and bronchi?
- Q2. Do you agree that only small droplets reach the alveoli?
- Q3. What is the optimal droplet size for aerosol delivery to the alveoli?
- Q4. What proportion of nebulized medication reaches at least the trachea?

In some questions, some words reflecting frequency were mentioned and their definitions were as follows: never, excep-

tionally (<5 patients/year), usually (5–12 patients/year), or frequently (>1 patient/month).

### Statistical analysis

Qualitative variables were expressed as *n* (%) and compared between groups using the chi-square test. The 95% confidence interval (CI) of proportions was calculated for the main variables of aerosol therapy. A *P*-value <0.05 was considered to indicate statistical significance. Fisher's exact test was used to compare rates between multiple groups. All statistical analyses were performed using SPSS 16.0 software (IBM Corporation, Somers, NY, USA).

## Results

### Study respondents

A total of 2203 medical staff who regularly worked in the ICUs completed this questionnaire (9.0% missing data); 87.7% of the participants were doctors. This sample covered various grades of hospitals across 30 provincial administrative areas in China. Most respondents claimed that they often (>5 patients/year) administered aerosolization therapy (65.4% in IMV and 73.4% in NIMV); only a few respondents refused to provide aerosolization during MV [Figure 1](#).

### Aerosolization devices

In all, 150 (6.8%) and 103 (4.7%) of the 2203 respondents reported never using aerosol therapy during IMV and NIMV, respectively. Practitioners in the ICU were more likely to use ultrasonic atomizer (50.7%) and jet nebulizer (48.6%), followed by hand-held devices (15.1%) and vibrating mesh nebulizer (12.7%).

### Drugs

Bronchodilators (65.8%) and steroids (66.3%) were the most frequently aerosolized drugs during MV [[Table 1](#)]. Mucolytic agents (49.0%) and anti-infective agents (35.8%) were also commonly used in ICU patients. Albuterol was the most commonly used bronchodilator in this study (61.8%), followed by ipratropium (54.8%) and terbutaline (54.5%) [[Table 1](#)]. Budesonide was the most commonly used drug among steroids (50.7%). Although some studies reported atomization treatment of antibiotics, the experience of antibiotics during atomization was relatively low in our study [[Table 1](#)].

### Ventilator settings and circuit

Some respondents (721, 32.7%) reported that they never changed the ventilator settings because of nebulization, whereas 1203 (54.6%) respondents always tried to change them. The rest of the respondents were uncertain about this problem. The most common position of the nebulizer for small-volume nebulizer was placed at the inspiratory limb (67.6%), while 72.7% of them reported placing the nebulizer just after the Y piece. Further, 27.3% of the respondents retained the connection tubing between the Y piece and the tracheal tube in place during nebulization. Only 5.6% of respondents reported placing a filter on

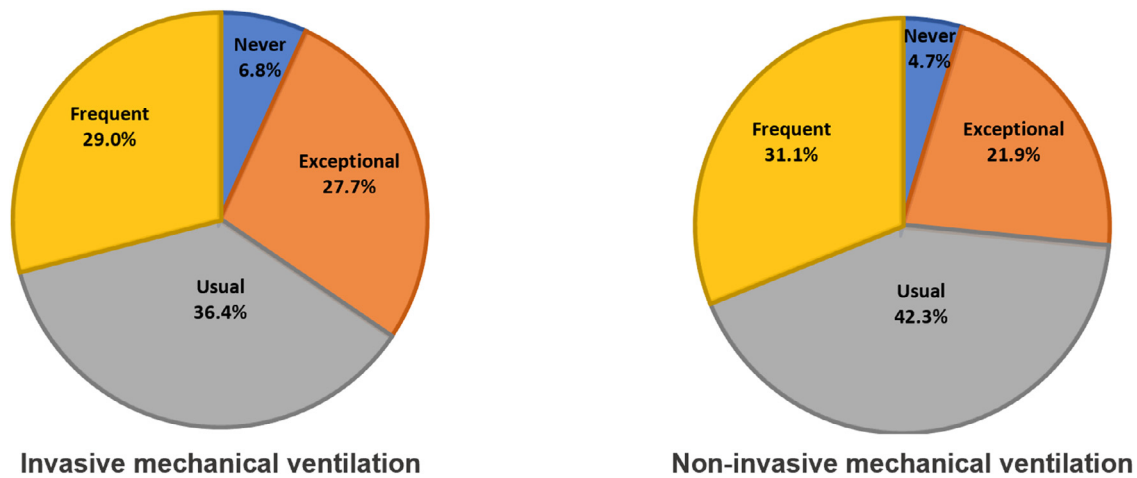


Figure 1. Frequency of atomization treatment during mechanical ventilation.

Table 1  
Drug classes to be aerosolized during MV (n=2203).

Drug class	Usage situation
Bronchodilators	1318 (65.8)
Ipratropium	1098 (54.8)
Albuterol	1237 (61.8)
Epinephrine	670 (33.5)
Terbutaline	1091 (54.5)
Fenoterol	441 (22.0)
Formoterol	324 (16.2)
Atropine	108 (5.4)
Steroids	1327 (66.3)
Budesonide	1116 (50.7)
Methylprednisolone	799 (36.3)
Beclomethasone	640 (29.1)
Dexamethasone	746 (33.9)
Betamethasone	511 (23.2)
Fluticasone	337 (15.3)
Hydrocortisone	746 (33.9)
Anti-infective agents	717 (35.8)
Colistin	377 (17.1)
Tobramycin	620 (28.1)
Amikacin	708 (32.1)
Gentamicin	612 (27.8)
Amphotericin B	470 (21.3)
Vancomycin	240 (10.9)
Pentamidine	278 (12.6)
Imipenem and cilastatin	199 (9.0)
Netilmicin	177 (8.0)
Ampicillin	202 (9.2)
Cefazolin	210 (9.5)
Ribavirin	132 (6.0)
None	9 (0.4)
Analgesics	535 (26.7)
Mucolytic agents	981 (49.0)
N-acetylcysteine	1007 (45.7)
Ambroxol	672 (30.5)
Chymotrypsin	385 (17.5)
Others	139 (6.3)
Ionic solutions	376 (18.8)
Other	97 (4.8)

Data are presented as n(%).

the expiratory limb, and others thought it was not necessary to change the place of the nebulizer. More than half of the respondents (62.7%) agreed to turn off the heated humidifier during nebulizer therapy, and the remaining respondents thought this was unnecessary Figure 2.

### Knowledge and opinions

Responses to the four questions about knowledge and beliefs are presented in Figure 3. More than half the respondents knew the relationship between droplet size and proximal-to-distal deposit ratio, but most respondents failed to answer optimal droplet size during nebulization and the proportion of nebulized medication that reached at least the trachea (Q1, Q2, and Q3) Figure 3. Only one-third of all respondents knew the proportion of nebulized medication that at least reached the trachea (Q4). There were significant differences among respondents from different levels of hospitals, with different technical titles and/or working hours. In general, respondents from tertiary hospitals, with higher technical title or longer experience tended to have better accuracy than those from primary hospitals or with lower technical titles (P<0.050) [Table 2]. There was a significant difference in atomization knowledge among different provinces (P<0.050). Given that we defined accuracy of 60.0% as an acceptable accuracy level, the top five provinces that reached the acceptance line were Zhejiang (86.7%), Shanghai (82.5%), Beijing (79.6%), Jiangsu (76.3%), and Guangdong (72.1%).

### Discussion

This study investigated the current practice of nebulizer therapy during MV among a nationwide panel of ICU staff in Chinese mainland. Despite a high proportion of atomized treatment with bronchodilators and steroids during MV, physicians' knowledge appeared limited on specific issues, and there was an obvious gap between junior physicians from non-tertiary hospitals and senior physicians from tertiary hospitals. The differences among provinces were also significant.

Aerosol therapy is frequently used in patients undergoing NMV or IMV, and bronchodilators and steroids were the most common drugs used in atomization, which were similar to previous surveys in Europe.<sup>[10,11]</sup> Few antibiotics were reported as relatively frequently nebulized since recent studies did not show strong evidence for antibiotic atomization in ICU patients.<sup>[14,15]</sup> Ultrasonic atomizer and jet nebulizer were the most commonly used atomization devices in the ICU, and though a vibrating

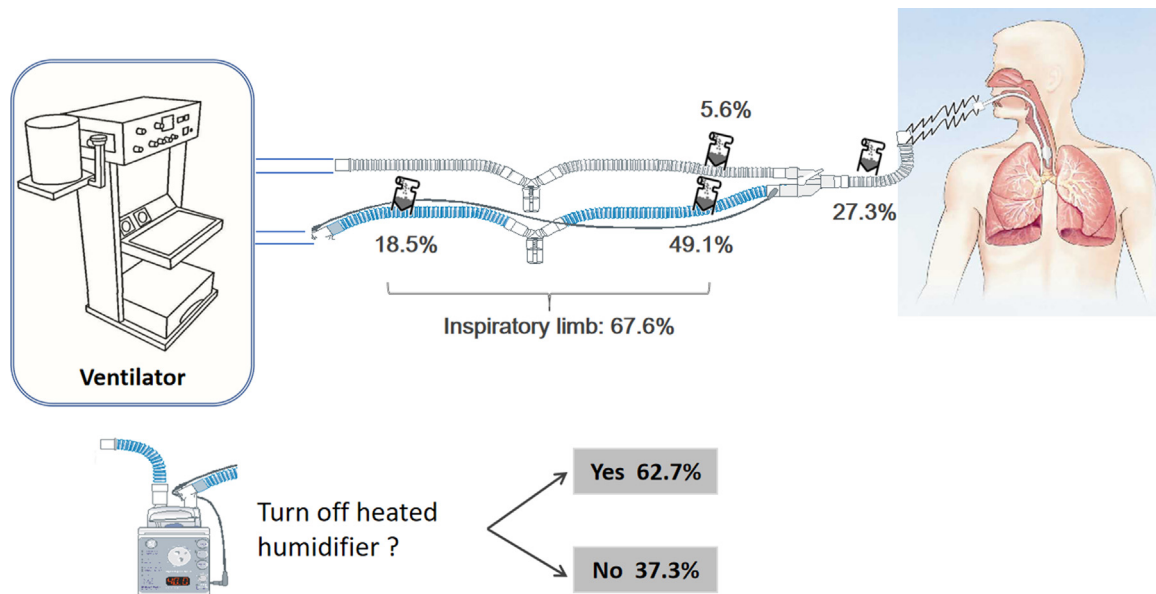


Figure 2. Main determinants of aerosol set-ups used in intubated patients. The values indicate the percentage of respondents (n = 2203).

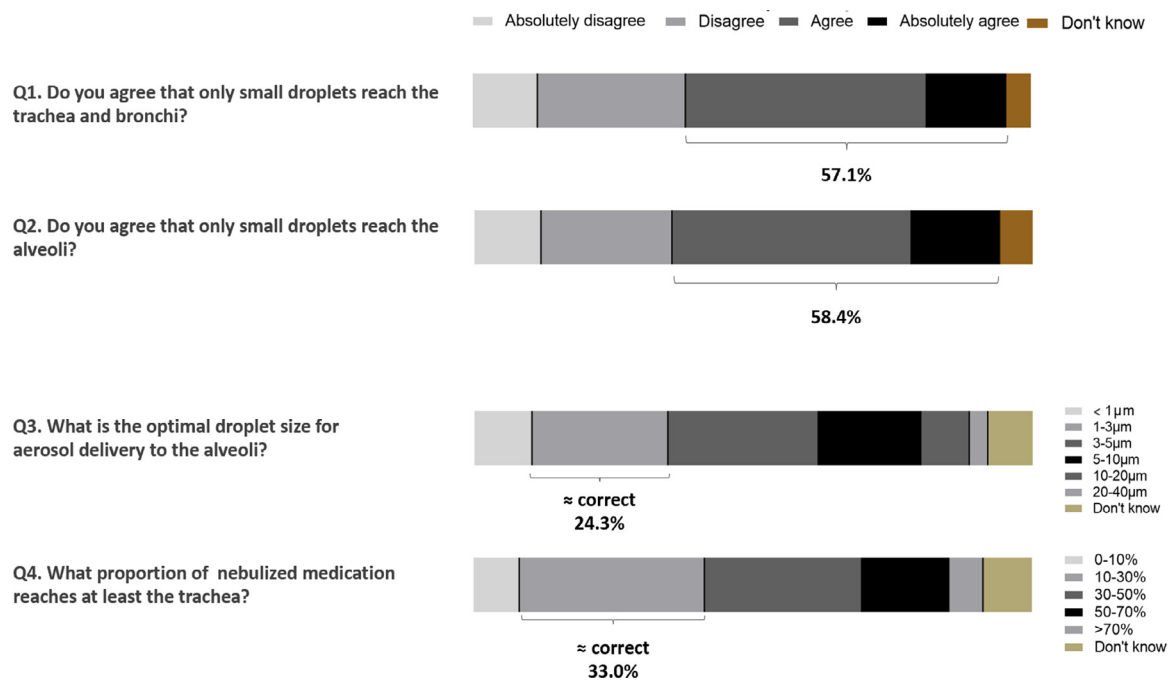


Figure 3. Droplet size and pulmonary deposition (n=2203). Data are presented as the percentage of respondents.

Table 2 Differences of knowledge and opinions among different groups. Data are presented as n(%).

Category	Q1 correct (n = 1253)	P-value	Q2 correct (n = 1277)	P-value	Q3 correct (n = 588)	P-value	Q4 correct (n = 615)	P-value
Hospital type		<0.001		<0.001		<0.001		<0.001
Tertiary hospital (n=796)	491 (61.7)		523 (65.7)		351 (44.1)		402 (50.5)	
Non-tertiary hospital (n=1398)	762 (54.5)		754 (53.9)		237 (17.0)		213 (15.2)	
Technical title		<0.001		<0.001		<0.001		<0.001
Resident (n=939)	322 (34.3)		315 (33.5)		121 (12.9)		124 (13.2)	
Attending physician (n=829)	652 (78.6)		592 (71.4)		307 (37.0)		234 (28.2)	
Chief physician (n = 426)	279 (65.5)		370 (86.8)		160 (37.5)		257 (60.3)	
Working years		<0.001		<0.001		0.012		0.718
<5 (n = 737)	279 (37.9)		324 (44.0)		173 (23.5)		203 (27.5)	
≥5 (n = 1457)	974 (66.8)		953 (65.4)		415 (28.5)		412 (28.3)	



mesh was reported with higher nebulization efficiency,<sup>[16]</sup> it was still infrequently used in many ICUs.

In recent years, many studies have summarized specific ventilator settings, and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) has recommended the use of specific ventilator settings during nebulization, which includes the use of a volume-controlled mode using a constant inspiratory flow, a respiratory rate of 12–15 beats/min, a tidal volume of 8 mL/kg, an inspiratory:expiratory (I:E) ratio of 50%, an inspiratory pause of 20%, and a positive end-expiratory pressure of 5–10 cmH<sub>2</sub>O. These measures can help to improve therapeutic efficiency.<sup>[17–19]</sup> However, there was still a certain percentage of respondents who refused to change ventilator settings and turn off the heated humidifier during nebulizer therapy. Only 49.1% of respondents knew the appropriate position for a nebulizer. The correct proportion was even lower than a similar survey conducted in Europe 7 years ago.<sup>[10]</sup> Our findings also demonstrated a lack of specific knowledge among ICU physicians in China regarding droplet size and optimal implementation of aerosol therapy during MV. Therefore, efforts to improve the awareness of standard aerosol therapy practice are warranted.

Our study included ICU physicians from different levels of hospitals and different provinces, with different working experience and technical titles. The results of our survey showed considerable gaps between different groups regarding specific nebulization knowledge. Physicians from tertiary hospitals, with higher technical titles or longer working years, seemed to have more knowledge reserve.<sup>[19]</sup> More training on nebulization treatment faced by basic-level hospitals and young ICU physicians are needed to bridge the gap in specific knowledge.

## Limitations

Because our study was designed as a questionnaire survey, there are some limitations concerning data interpretation. First, respondents may have presented an inaccurate representation of the real practice of nebulization as performed during their clinical work. Second, although the survey was anonymous, it is possible that respondents may have responded in accordance with the literature rather than describing their real practice and beliefs. Third, the results of our survey were similar to a previous study in Europe, which demonstrated the same lack of atomization knowledge in physicians and the gap between scientific evidence concerning optimal nebulization techniques during MV and actual clinical operation.<sup>[11]</sup> More profound findings have not been presented, and this may be explained by the fact that the questionnaires are similar. More detailed questionnaires are needed in the future to describe the professional level of practitioners in China. A prospective observational study recording actual ICU practices may be needed to provide more objective data about nebulization techniques during MV in China.

## Conclusions

Aerosol therapy was commonly used during MV, and the most frequent drugs were bronchodilators and steroids. Scientific knowledge about the optimal implementation of aerosol therapy during MV seemed infrequently applied, which might lead to dangerous practices in the ICU. There was a knowl-

edge gap between physicians of different levels of hospitals and work experience years. Hence, more educational and training programs are needed to focus on simplifying bench-to-bedside knowledge transfer.

## Ethical approval and consent to participate

Not available.

## Availability of Data and Material

The datasets during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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## Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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