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Major Article

Risk factors of lower respiratory tract infection in patients after tracheal intubation under general anesthesia in the Chinese health care system: A meta-analysis

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Background: Lower respiratory tract infection (LRTI) after tracheal intubation under general anesthesia poses a serious threat to worldwide health care systems, especially those in developing countries. However, a significant number of studies have found inconsistent results in their investigation of the corresponding risk factors.

Methods: Relevant articles published up to September 2015 were retrieved from PubMed, Ovid, Embase, China National Knowledge Infrastructure, Chinese Biological Medical Database, China Science and Technology Journal Database, and Wanfang Data. The *z* test was used to determine the significance of the pooled odds ratio (OR). ORs and 95% confidence intervals were used to compare the risk factors of LRTI after intubation under general anesthesia.

Results: Fifteen case-control studies that included 27,304 participants were identified. We identified the following variables as independent risk factors: duration of general anesthesia >3 hours (OR, 2.45), age >60 years (OR, 2.35), normal endotracheal tube (OR, 1.63), deep intubation (OR, 2.66), unpracticed intubation (OR, 2.61), postoperative extubation time >2 hours (OR, 3.76), smoking history (OR, 3.02), chronic respiratory disease history (OR, 2.30), incomplete extubation indication (OR, 3.54), thoracic or craniocerebral surgery (OR, 1.90), and emergent surgery (OR, 2.54).

Conclusions: Eleven risk factors, including surgery, anesthesia, and health condition, were related to LRTI after intubation under general anesthesia. Given the limitations of this study, well-designed epidemiologic studies with a large sample size should be performed in the future.

BACKGROUND

With China being a developing country, its hospital infection research only began recently and therefore lags behind that of other developed countries.[1] In recent years, postoperative infections are still common hospital infections in China; however, much more emphasis has been put on infection control.[2] The main risk factors of postoperative infections explored by researchers that were found to be related to nosocomial infection after surgery are as follows: (1) patient factors (eg, advanced age combined with diabetes and preoperative nutritional status); (2) surgery factors, including surgery time and site; and (3) anesthesia factors (eg, American Society of Anesthesiologists grade ≥3).[3-5] As the currently most secure and widely used method for administering anesthesia, endotracheal intubation has advanced in terms of technology and infection control.[6,7] However, lower respiratory tract infection (LRTI) after anesthesia remains a common infection that increases hospital mortality, inpatient health care costs, and hospital duration. These effects impose a serious burden on patients and on the whole health care system. As a result of the active participation of Chinese researchers and anesthetists in the prevention and control of postoperative infections, an increasing number of studies have been conducted, but the results are inconsistent and controversial. To some extent, LRTI occurrence after tracheal anesthesia is associated with intubation

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strategy and the health conditions of patients. In an attempt to overcome the limitation of single case studies, we performed a meta-analysis involving 15 subjects to provide a precise and comprehensive estimation of LRTI after tracheal intubation under general anesthesia.

METHODS

A meta-analysis of observational studies on risk factors related to LRTI after intubation under general anesthesia was undertaken according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (http://www.prisma-statement.org). The methodology included data source collection, inclusion criteria, exclusion criteria, data extraction, quality assessment, and statistical analysis.

Data source collection

A systematic search of PubMed, Ovid, Embase, China National Knowledge Infrastructure, Chinese Biological Medical Database, China Science and Technology Journal Database, and Wanfang Data was performed in English and Chinese to identify articles published up to September 2015 that explored the risk factors of LRTI after tracheal intubation under general anesthesia. The search terms included the following: (general anesthesia OR inhalation anesthesia OR anesthesia) AND (respiratory tract infections OR pulmonary infection OR lung infection OR pneumonia OR bronchitis) AND (intubation OR tracheal intubation). The references to all identified published works were entered into a reference management software program (EndNote X6; Thomson Reuters, Toronto, ON, Canada).

Inclusion criteria

The initial screening of titles and abstracts was independently performed by 2 reviewers (X.X. and M.L.). A second screening was completed through a full-text review by the same reviewers. Then, we compared the screened studies to determine whether they were in accordance with the cross-check method. Controversial issues were addressed by a third reviewer (Y.L.) when necessary.

The inclusion criteria were as follows. First, the study must have been conducted in relation to the risk factors of LRTI after tracheal intubation under general anesthesia. Second, the study must have been designed as a case-control study, a cohort study, or a randomized controlled trial study. Third, the definition and diagnostic criteria for LRTI must have been defined as the presence of at least 1 respiratory symptom (cough, sputum production, dyspnea, tachypnea, or pleuritic pain) along with at least 1 finding during auscultation (rales or crepitation) or 1 sign of infection (core body temperature >38.0°C, shivering, or leukocyte count $>10 \times 10^9$/L or $<4 \times 10^9$/L cells), independent of antibiotic pretreatment.[8] Finally, the study must have been published in English or Chinese.

Exclusion criteria

Studies were excluded if they were (1) identical studies retrieved from different databases, (2) animal studies, (3) case reports or reviews, and (4) studies that did not provide sufficient information to allow the calculation of odds ratios (ORs) and 95% confidence intervals (CIs).

Data extraction

Two reviewers (X.X. and X.Y.) independently extracted the data using a unified datasheet. The extraction results were evaluated by other reviewers (S.L. and Y.Q.). The extracted information included the first author, study time and region, year of publication, and number of cases and control patients. Different opinions regarding data abstraction were resolved through discussion.

Quality assessment

Quality assessment was conducted for each study according to the Newcastle-Ottawa Scale[9] for the selection of cases (4 items, 4 points), comparability of cases and controls (1 item, 2 points), and ascertainment of exposure to risks (3 items, 3 points) (9 points in total). Low-quality research was scored 0-4 points, whereas high-quality research was scored 5-9 points.[10] The quality of each study was assessed by 3 reviewers (X.Z., J.X., and J.Q.) independently. Disagreements on scoring were resolved through discussion among the research group until consensus was reached.

Statistical analysis

A meta-analysis was performed using Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Danmark). The heterogeneity among the results of the included studies was evaluated via χ^2 and I^2 statistic tests. The random effects model was used once the effects were found to be heterogeneous ($I^2 > 50\%$ or $P < .05$). Otherwise, the fixed effects model was used. The z test was used to determine the significance of the pooled OR. We used ORs and 95% CIs to compare the risk factors of LRTI after intubation under general anesthesia. The results were considered to be statistically significant when $P < .05$. In addition, publication bias was examined using Begg test and Egger test performed on the software Stata 11.0 (StataCorp, College Station, TX). Sensitivity analyses were conducted by omitting individual studies sequentially and by comparing the P values of the pooled ORs for the random and fixed effects models. The overall population rate was used as a substitute for the pool exposure rate (P_e) of the controls to calculate the population attributable risk proportion (PARP), which is written as follows: $\mathrm{PARP} = P_e(\mathrm{OR} - 1)/P_e(\mathrm{OR} - 1) + 1$.

RESULTS

Study description

A total of 1,141 potentially relevant articles published up to September 2015 were systematically identified through an electronic database search. After screening the titles and abstracts, we retained 102 studies, excluding duplicates, studies without intubation and risk factors, animal tests, reviews, and case reports. Among these studies, 87 works were excluded via full-text screening because they did not match the inclusion criteria. Finally, 15 studies were included in the meta-analysis (Fig 1). The basic characteristics of the 15 studies are presented in Table 1. These studies were published from 2003-2015 in Chinese and were conducted in 8 different provinces in China. All studies were used as case-control and assessed as high-quality research.

Incidence of LRTI

A total of 27,304 participants (2,454 cases and 24,850 controls) were identified in our study. The incidence of LRTI after tracheal intubation under general anesthesia ranged from 2.8%-24.7% (Table 1).

Risk factors of LRTI

The risk factors of LRTI after tracheal intubation under general anesthesia in the meta-analysis are shown in Table 2. The I^2 statistic was calculated to determine the size of heterogeneity.[11] We