

The Effect of Povidone-Iodine for The Prevention of Pneumonia

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Abstract. Background: Pneumonia poses a significant health threat and adversely affects the well-being and recovery of patients, particularly the elderly. With the growing emphasis on preventive healthcare and the rise in population aging, the prevention of pneumonia has become increasingly crucial. Povidone-iodine, a readily available and potent bactericidal disinfectant, has garnered attention for its potential in preventing pneumonia through oral disinfection. Objective: To evaluate the preventive effect of povidone-iodine on pneumonia. Methods: This article systematically searched for published studies in English and Chinese database (i.e., the PubMed, China National Knowledge Infrastructure) between 2004 and 2024. This study included studies reporting the clinical application and effect of povidone iodine and the incidence of pneumonia. The raw data from these studies were pooled into the analysis of this article. The statistical analyses used in this study were performed using Stata version 17.0 (Stata Corp LLC, College Station, TX). Results: Fifteen studies were included in the study analysis. Nine studies showed that povidone-iodine reduced the incidence of pneumonia compared with saline, placebo, and oral care (RR: 0.39, 95% CI: 0.23-0.65, $Z = 0.279$, $P = 0.005$, $I^2: 63.5\%$). The remaining 4 articles all showed the positive effect of povidone-iodine on the prevention of pneumonia. Two other studies showed that chlorhexidine oral care was more effective than povidone-iodine in preventing pneumonia, but only one study was statistically significant. Conclusion: The use of povidone iodine for gargling, mouth and nose care is a protective factor against pneumonia. It has important implications for pneumonia prevention strategies.

Keywords: Povidone-iodine; pneumonia; preventive healthcare.

1. Introduction

In the 21st century, there has been a shift from an emphasis on economic development to a focus on personal health, making health the foremost priority for individuals. The 21st century has become an era for people to pursue health, and preventing disease has become increasingly important. However, studies have shown that as life expectancy increases, healthy, disease-free life (healthy span) does not increase as much as life expectancy [1].

Pneumonia is an infection of the small air sacs (alveoli) and surrounding tissue in the lungs. Pneumonia can be divided into community-acquired pneumonia, hospital-acquired pneumonia, aspiration pneumonia, obstructive pneumonia and other pneumonia.

1.1. Global burden of pneumonia

In 2019, pneumonia will cause nearly 2.5 million deaths worldwide, making it the fourth leading cause of death worldwide. It has a high incidence and mortality and is one of the most expensive diseases requiring hospitalisation [2]. Among these, pneumonia is a major cause of morbidity and mortality due to infection in the elderly population [3]. The management of pneumonia is an important issue in geriatrics. Elderly patients are at a higher risk of developing pneumonia due to several factors. These include impaired vomiting reflex, reduced mucociliary function, weakened immunity, impaired febrile response, and varying degrees of cardiopulmonary dysfunction [4]. Pneumonia is usually caused by the upper respiratory tract inhaled microorganisms into the lungs, and people's airways and alveoli cannot avoid contact with various microorganisms, especially long-term need to use ventilator patients, more likely to cause infection ventilator-associated pneumonia (VAP). This situation is one of the most common hospital infections in the intensive care unit (ICU), affecting one-third of the need to use ventilator patients [5]. Meanwhile, the prevalence of the novel coronavirus pneumonia epidemic has greatly increased the incidence of pneumonia. The World

Health Organisation (WHO) declared COVID-19 a global pandemic on 11 March 2020 [6]. By 2020-2021, it had affected more than 2 billion people worldwide and caused more than 4 million deaths [7]. Since SARS-CoV-2 can survive atomisation for three hours under experimental conditions, both in plastic and stainless steel, it can survive for more than 72 hours [8]. This greatly increases the likelihood that medical workers [8] and children will be infected. Given the high prevalence and mortality of pneumonia in the general population, it is particularly important to find simple and effective ways to prevent pneumonia.

1.2. Existing preventive measures for pneumonia

At present, the main measures used to prevent pneumonia are as follows: to begin with, general hygiene measures—like donning face masks and avoiding droplet contact—are essential for combating respiratory infections worldwide. Secondly, clinicians need to be extremely cautious when dealing with different populations. Immunosuppressive therapy and oral steroids are risk factors for pneumonia, and clinicians should avoid inappropriate medication. Thirdly, respiratory physiotherapy should be used to teach people deep breathing exercises and to coordinate breathing. Fourth, pay attention to oral hygiene. Poor oral hygiene promotes the accumulation of dental plaque, and the number of periodontal bacteria in people aged 85 years increases with the number of teeth [9]. In 2008, a comprehensive review analysed the relationship between pneumonia risk and oral health and found that 1 in 10 deaths in individuals living in institutions could have been prevented with proper and regular oral hygiene [10]. Among the above-mentioned preventive measures, mask use is suitable for all populations, but it lacks specificity and effectiveness. Both drug prevention and physical precautions need to be carried out under the guidance of professionals, so these measures are not very practical for the general population without professional knowledge. Oral hygiene, on the other hand, is more suitable for all groups of people, and everyone can prevent pneumonia by making small changes to their lifestyle. However, there is no clear evidence of a link between oral hygiene and pneumonia mortality.

1.3. Povidone iodine as a potential preventive approach

Bacterial infection of the lungs caused by oropharyngeal contents and the introduction of pathogenic bacteria is a major cause of pneumonia. Povidone-iodine is an extremely powerful, broad-spectrum bactericidal disinfectant that works wonders against mould spores, bacteria, fungus, and viruses. This product has low skin irritation, low toxicity and long-lasting action. Safe and easy to use. One of the most effective antimicrobial agents for lowering the risk of respiratory tract infections is povidone iodine [4]. Gargling with povidone-iodine four times a day has been shown to reduce the incidence of upper respiratory tract infections. Povidone-iodine is useful in decreasing the body's concentration of *Haemophilus influenzae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* (including MRSA) in cases of chronic respiratory infections. The Respiratory Management Guidelines Committee of the Japanese Respiratory Society has shown that the use of povidone-iodine gargle by inpatients and medical staff can prevent hospital-acquired pneumonia [11]. Oral interventions with povidone-iodine may be effective in preventing and treating pneumonia in the elderly. However, there are also studies showing that the use of povidone-iodine is not associated with the prevention of pneumonia [12]. Therefore, the effectiveness of povidone-iodine in avoiding pneumonia is not well-established.

On the basis of the above, the aim of this review was to summarise the available evidence on the effect of povidone-iodine in the prevention of pneumonia.

2. Methods

2.1. Search strategy

In early March 2024, approximately 15 research papers were extracted from PubMed and China National Knowledge Infrastructure. These publications contain at least one of the terms: povidone-

iodine, oral cavity, and pneumonia. These papers were comprehensively considered by scanning the abstract to obtain relevant information related to povidone iodine and population. The second round of elimination measures was undertaken by reading the publications in detail and retaining the papers that provide useful information for this review.

2.2. Inclusion & Exclusion Criteria

The inclusion criteria: (1) articles published in the last 20 years, (2) articles on povidone-iodine and pneumonia, (3) the study population was people who did not have pneumonia, (4) povidone-iodine was used in the intervention studied, (5) the results of the included articles included data on the prevalence of pneumonia in the study population. Exclusion criteria were: (1) all papers published in languages other than English and Chinese, (2) people with pneumonia, (3) papers without any data on povidone-iodine for the prevention of pneumonia, (4) papers with duplicate information, (5) the types of articles are reviews, letters, comments, corrections.

2.3. Data Extraction

Data collected for each study were as follows: author, year of publication, total number of subjects, incidence of pneumonia in the population treated with povidone-iodine, and incidence of pneumonia in the control group. In addition, other less important information such as ratio of males to females in the population, study site.

2.4. Statistical analysis

Stata version 17.0 is used for analysis. A pooled effect size (RR) with a 95% confidence interval (95% CI) was calculated to assess the relationship between povidone-iodine use and pneumonia infection. The P -value <0.05 was statistically significant. Heterogeneity was assessed as I^2 and if heterogeneity was significant ($I^2 > 50\%$), a random-effects model was used.

3. Result

217 articles were obtained by database search and two articles was manually searched. The one duplicate record was then eliminated. 173 papers were deemed unsuitable for this investigation after the titles and abstracts of the articles were screened. Upon reviewing the complete texts of the 42 surviving articles, 9 of the studies were of the Comment/Letter/Correction study type; 7 of the studies involved populations that were not pneumonia-free; 8 of the studies neglected to mention the outcomes of pneumonia; 4 of the studies lacked data; and 2 of the studies dealt with other subjects. After reading the full text, the qualitative analysis excluded none of the 15 selected studies. Fig. 1 describes the process of retrieval, identification, inclusion, and exclusion of the studies.

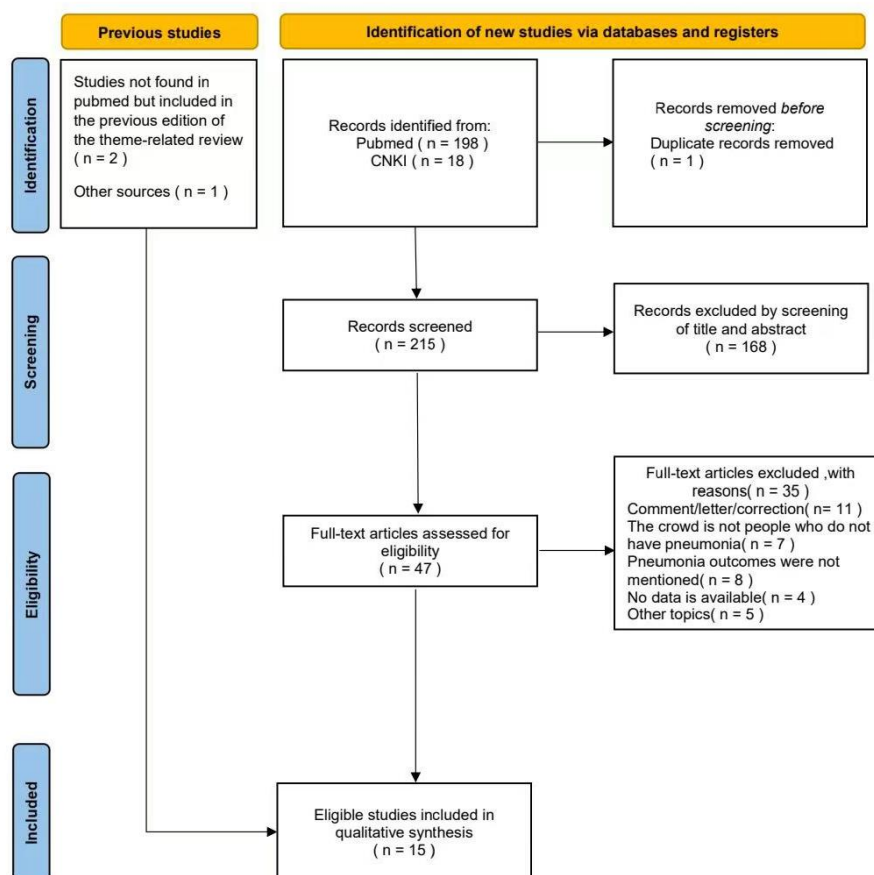


Fig. 1 Study selection flowchart for analysis

These studies were published between 2004 and 2024, and patients from Manila [13], Japan [14][16], France [15][18], India[17], Singapore[19] and China[20-27] were included in these studies. The ethics committees of their respective institutions or hospitals approved all selected studies that also provided informed consent before recruiting patients.

Four of the 15 studies included were blinded studies. The rest did not attempt to blind their participants, however the outcome assessors, data entry staff, and statisticians were largely blind to the assignment group. The povidone-iodine solution used had multiple concentrations of 0.02% or 0.1% or 0.35% or 0.45% or 0.5% or 1% or 10%, and all studies also used povidone-iodine, but mainly in oral care. There was considerable variation in treatment frequency, with the longest trial lasting five months.

All the included studies [13-27] were Randomized Controlled Trial (RCT) designed. The study population in this article was > 10 years old and initially without pneumonia-related diseases. A total of 4436 participants took part in the study, of whom 1369 were in the intervention group and 3067 in the control group. The most people are men. The essential characteristics of the studies included are presented in Table 1.

From the use of povidone iodine, all of the included literature is oral care, including but not limited to oral lavage, gargling, brushing, throat spray, oral flushing and scrubbing. In terms of control type, nine articles used the saline or placebo as the control group of povidone-iodine group. Analysis of these studies showed an association between the use of povidone-iodine care for the prevention of pneumonia (RR=0.39, 95% CI =0.23-0.65; I² =63.5%, Fig. 2). In the remaining six articles, SATO (2006) reported that oral care such as povidone iodine for gargling, brushing teeth, special brush teeth and tongue back was better at preventing lung lesions than gargle with only povidone iodine. Gupta

(2014) indicated that povidone-iodine mouthwash was inferior to chlorhexidine oral care in preventing ventilator-associated pneumonia (VAP), although this conclusion did not reach statistical significance. Set (2021) said that the use of povidone-iodine throat spray is highly safe, has fewer side effects, and has a positive effect on preventing COVID-19. Xu (2022) indicated that the use of povidone-iodine mouthwash to prevent acquired pneumonia was better than the compound borax mouthwash for oral care. According to the study of Yang (2012), oral care with 0.5% povidone iodine was more effective to prevent and reduce ventilator-associated pneumonia (VAP) in patients with transorotracheal intubation. Xu (2012) indicated that the 0.12% oral care method has advantages over the 0.5% povidone-iodine method in preventing hospital-acquired pneumonia.

Table 1. Study characteristics of the included studies

Author (year)	Country	Participants	Sample size	Mean age	Gender (M/F)	Povidone-iodine content	Using methods of povidone-iodine	Modality of control/intervention in the control group	Lung condition	Main outcome
Chua (2005)	Manila	ICU patients.	42	53.0	25/17	1%	Nurses give oral lavage every 8 hours.	Placebo-controlled	VAP	The use of povidone-iodine oral rinse as prophylaxis against VAP shows a trend towards benefit
SATO (2006)	Japan	With diseases other than lungs	29	74.9	19/11	0.02%	Dentures are cleaned with a special toothbrush, rinsed and brushed with 0.02% Povidone iodine, and the back of the tongue is cleaned with a tongue brush.	Only povidone-iodine gargle is performed.	Dry or moist rale pulmonary sounds	When older people have digestive system surgery, receiving post-operative dental care reduces the amount of bacteria in the mouth cavity.
Seguin (2006)	France	With severe head trauma.	98	NA (≥18)	75/23	10%	20 mL of 10% povidone-iodine is progressively injected into the oral cavity	①Saline group ②Blank control group	VAP	For individuals who have suffered severe head trauma, using povidone-iodine on a regular

							and pharyngeal cavity with a 60 mL syringe and aspirated at regular intervals every 4 hours.			administration may be a useful tactic to reduce the incidence of ventilator-associated pneumonia.
Ishikawa (2008)	Japan	Living in nursing homes	202	81.8	49/53	0.35%	Gargled with 0.35% povidone iodine once a day after lunch for the first 2 mos.	①Facility A:a dental hygienist performs professional oral health care services once a week for 5 months; ②Facility B:the residents have not received professional care in the first 2 months. For the next 3 months, they were professionally cared for by a dental hygienist once a week.	Aspiration Pneumonia	An important strategy for preventing aspiration pneumonia in dependent older adults is weekly professional mechanical oral cleaning, rather than daily chemical oral disinfection.
Li (2009)	China	With oral mechanical ventilation	60	NA (10-70)	40/20	0.5%	Oral flushing and scrubbing, the amount of irrigation is 2~3ml/time, and the irrigation solution is sucked out with a suction device while rinsing.	Normal saline	VAP	The application of 0.5% povidone-iodine solution in oral mechanical ventilation patients can effectively reduce the occurrence of VAP.

Gao (2012)	China	With severe burns	97	NA (21 - 68)	65/32	0.1%	Oral care.	Normal saline	VAP	Povidone-iodine for oral care can effectively reduce bacterial colonization in the oropharynx and trachea during mechanical ventilation in patients with severe burns, and can effectively reduce and delay the occurrence of VAP
Yang (2012)	China	Mechanically ventilated through orotracheal intubation	50	NA (30 - 85)	30/20	0.5%	Oral scrubbing and oral irrigation.	Used oral care with Koutaixing	VAP	Use 0.5% Povidone-iodine for oral care is more effective than Compound Chlorhexidine Gargle for oral care prevention and VAP reduction in patients with orotracheal intubation
Xu (2012)	China	ICU	58	59.0	36/22	0.5%	Oral irrigation and oral wiping.	0.12% Chlorhexidine oral care	VAP, Hospital-acquired pneumonia	In reducing hospital-acquired pneumonia, 0.12% chlorhexidine oral care was also better than 0.5% povidone-iodine solution.
Gupta	India	Requiring more than 72	70	48.3	40/30	NA	Povidone iodine oral care.	Chlorhexidine group	VAP	Chlorhexidine mouthwash is superior to

(2014)		hours of mechanical ventilation in ICU.								povidone-iodine mouthwash in preventing VAP, but more studies with larger sample sizes are needed.
Seguin (2014)	France	Severely brain-injured or cerebral hemorrhage	150	48.0	128/43	10%	Before extubation or for 30 days, the solution is gradually injected into the mouth and pharynx cavity at regular intervals and aspirated every 4 hours.	Placebo-controlled	VAP	There is insufficient evidence that Povidone-iodine oral care prevents ventilator-associated pneumonia in high-risk patients.
Huang (2018)	China	With head injury and admitted to the surgical ICU for treatment	98	45.9	53/45	NA	Oral disinfection.	① Natrue saline group (60 ml) ③ Blank control groups	VAP	Compared with the saline group and the control group, the incidence of VAP decreased in the povidone-iodine group.
Seet (2021)	Singapore	Healthy migrant workers in quarantine	3037	33.0	All male	0.45%	Throat sprays a single dose; Povidone-iodine throat spray was self-administered three times daily (approximately 270 mg/day)	① Oral hydroxychloroquine; ② oral ivermectin; ③ oral zinc/vitamin C; ④ oral vitamin C	COVID-19	In young, healthy men, chemoprophylaxis with oral hydroxychloroquine or povidone-iodine throat spray was more effective than oral vitamin C in lowering SARS-CoV-2 infection.

							for 42 days.			
Xu (2022)	China	Critically ill neurosurgical patients	100	50.0	54/46	NA	Oral care with povidone-iodine gargle.	Be treated with compound borax gargle for oral care	Acquired pneumonia	There was no significant difference in the incidence of acquired pneumonia between the observation group and the control group (P>0.05).
Ding (2023)	China	ICU endotracheal intubated patients	81	48.9	43/38	NA	Povidone-iodine gargle Oral care is given twice daily.	Saline oral care	VAP	Povidone-iodine gargle provides better oral hygiene, significantly improves oral health in ICU patients, and reduces oral-related complications and late-onset VAP.
Yang (2023)	China	undergoing spinal surgery	264	NA (≥60)	NA	0.5%	0.5% povidone-iodine gargle with 20 mL iodine disinfectant and rinse twice.	With 0.9% saline oral cleaning	Lower respiratory tract infect	Oral pretreatment with 0.5% povidone-iodine disinfectant before anesthesia can reduce the detection rate of oropharyngeal pathogens and reduce lower respiratory tract infection in elderly spinal surgery patients under general anesthesia.

Note:

NA: (Not available); VAP: (Ventilator associated pneumonia)

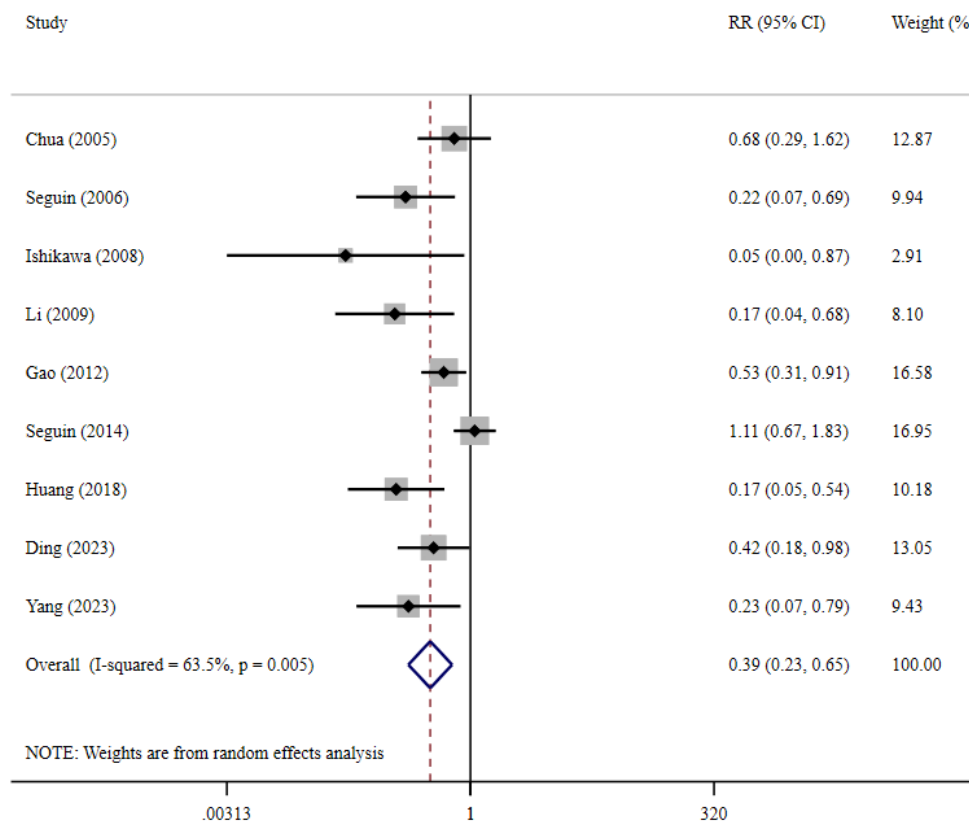


Fig. 2 Forest plot of the relationship between povidone-iodine group and control group (saline, placebo, oral care)

4. Discussion

Pneumonia usually begins when microorganisms from the upper respiratory tract are inhaled into the lungs, but sometimes an imbalance between the respiratory tract and the lungs, or the inhalation of microorganisms from the air that are carried to the lungs by the bloodstream, or the direct invasion of the lungs from a nearby site of infection can cause infection. As the inhalation of oropharyngeal fluid containing pathogenic microorganisms is one of the most important factors leading to the development of pneumonia, this study sought to achieve the effect of preventing pneumonia by reducing the risk of developing pneumonia through oral or nasal care with povidone-iodine.

4.1. The mechanism behind povidone-iodine for the prevention of pneumonia

An answer to the question of why povidone-iodine has the effect of preventing pneumonia. First of all, povidone-iodine is a drug that has no bactericidal activity in itself, and it mediates the oxidation of amino acids and nucleic acids in biological structures through free iodine transport to target cell membranes. This mechanism of action leads to intense microbicidal activity, including the destruction of the microbial cell membrane, the disruption of its metabolic pathways, and irreversible damage to pathogens. In addition, povidone-iodine also inhibits the release of various pathogenic agents. After these mechanisms, the consumed free iodine is replaced by povidone-iodine-bound iodine [11]. Secondly, the first step of respiratory tract infection is the adhesion and colonization of respiratory pathogens on the oropharyngeal mucosa [11]. Therefore, if povidone-iodine is used for oral cleaning care, the occurrence of respiratory tract infection is prevented in the first step.

4.2. Preventive effect of povidone-iodine

This study evaluated the preventive effect of povidone iodine against pneumonia. The results showed that the use of povidone iodine reduced the incidence of pneumonia compared with the saline, placebo and oral care without other drugs. At the same time, some other trials compared other medications with povidone iodine, and two articles suggested that povidone iodine had beneficial effects in preventing pneumonia; and two studies indicated that povidone iodine was less successful in avoiding pneumonia than chlorhexidine; however, only one of these two studies demonstrated statistical significance and did not refute the effectiveness of povidone iodine.

4.3. Effect of application methods on the effectiveness of prevention

Different ways of using povidone iodine can have different preventive effects. At present, the most common methods of use are mainly for the mouth and nose, such as nasal spray, nasal drops, mouthwash, throat spray, etc. Whether the operation of mouthwash is standardized has a great impact on the results of the study. According to a Japanese study, different people have different gargling habits [28]. In the study, povidone-iodine was used to gargle evenly over the entire mouth. If the supervision in the study is poor or the workers are not trained, some people will gargle according to their original habits, only to achieve the effect of washing part of the mouth, povidone iodine will not be evenly distributed in the whole mouth, and the effect of preventing pneumonia will be greatly reduced, which will have a great impact on the experimental results. Therefore, most of the literature included in this review had trained health professionals gargle the subjects, which greatly improved the validity and credibility of the study. Throat sprays, on the other hand, deliver the drug mainly to the mouth and throat, although this method cannot deliver the drug to the nasal cavity, but pharyngeal povidone iodine possibly can be re-distributed to the nasal cavity by the action of mucus and cilia, so the effect of throat spraying may be better than that of rinsing alone [29].

4.4. The positive effect of preventive measures on the healthy elderly care of the elderly in this study

The study population in this review ranged from children as young as 10 years old to 98 years old. Three of the articles were identified as elderly (60 years or older). If the effectiveness of povidone-iodine in preventing pneumonia can be established in this era of global ageing, it will be a good measure to prevent pneumonia in older people who are homebound. Older people often choose to be cared for at home because they like their familiar surroundings and some traditional ideas. As a result, some over-specialised precautions no longer apply to the elderly population. The use of povidone iodine for oral care has made it possible for older people to prevent pneumonia in their own homes. This method has opened up the idea of home care for the elderly to prevent pneumonia.

4.5. Improper use of povidone-iodine carries a risk of aspiration pneumonia

It is worth noting that some studies have found that povidone-iodine can also cause aspiration pneumonia. In the study of an (2011) [30], it was known that during the operation of a 16-year-old female patient with a fracture of the left upper jaw, the patient accidentally damaged the tube, resulting in air leakage, and the patient inhaled povidone-iodine, causing aspiration pneumonia. Choi (2014) [31] also had a similar pathology report. They performed a facial fracture reduction surgery for a 15-year-old woman with an air leak from the first intubation, although no abnormalities were found after the catheter was replaced. However, the patient still has aspiration pneumonia, so they suspected that the patient had inhaled povidone-iodine. In a report by Hitosugi (2019) [32], oral irrigation with povidone-iodine solution was performed in a 91-year-old patient before oral and maxillofacial surgery, but the patient aspirated during the process, resulting in chemical damage to the left trachea and bronchi and aspiration pneumonia. Most of these studies are case reports, and aspiration pneumonia is mostly caused by accidental aspiration during general anaesthesia or due to equipment damage and improper handling, and aspiration pneumonia caused by aspiration of povidone iodine during general anaesthesia is rare. Therefore, they were not included in this study.

However, this situation is worth noting in order to be safer to use povidone-iodine for mouth and nose care to prevent pneumonia in the future.

Further investigation of these phenomena reveals that the majority of aspiration pneumonitis is due to aspiration of gastric contents, and only a few cases are due to aspiration of povidone-iodine. In addition, aspiration occurred mostly due to the patient's lack of consciousness under general anesthesia, which is inconsistent with the situation in this study in which the study subjects were asked to rinse their mouths. However, inhale of povidone-iodine does lead to aspiration pneumonia. When povidone-iodine is inhaled into the lungs, it causes irritation to the lungs, causing inflammation of the lungs, which makes them more susceptible to bacterial infections. Moreover, as people age, their consciousness gradually changes, and the elderly become more likely to be aspirated. Therefore, it is necessary to understand the adverse consequences of inhalation of povidone-iodine, and it is necessary to avoid aspiration in future use. In clinical settings, doctors should be more cautious with povidone-iodine in patients who are unconscious, and raising the head of the bed by more than thirty degrees could be beneficial if needed.

4.6. Limitations

However, there are limitations. In this study, because it is about the preventive effect of povidone iodine against pneumonia, the specific types of pneumonia are not subdivided and the population is only defined as those who do not have pneumonia, and there is no too detailed limitation. About the use of povidone iodine for different types of pneumonia and different populations, there is no conclusion on which type of pneumonia or which population is better prevented due to the lack of relevant studies. In addition, in the forest plot analysis, two of the control groups were placebo controls, 6 were saline controls, and 1 was an unmedicated oral care control. The type of solution used in the controls was not too restrictive, so there may be differences.

In general, povidone-iodine is a safe and effective disinfectant, which has a certain effect on the prevention of pneumonia, but it is still necessary to pay attention to the operation specifications when using it to prevent aspiration.

5. Conclusion

Povidone-iodine may be a useful drug for preventing pneumonia, according to this review. This is because, the forest plot made from the data in the included literature shows that the RR value is <1 , which means that the risk of developing pneumonia with povidone-iodine for gargling or oral and nasal care is lower than that of the control group, which is negatively correlated. In general, the use of povidone iodine for gargling, mouth and nose care is a protective factor against pneumonia. It has important implications for pneumonia prevention strategies.

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