Aspiration Pneumonia and oral health: a critical review of literature

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ABSTRACT
Objective: to identify evidences in the scientific literature if mechanical or chemical oral hygiene can prevent aspiration pneumonia in hospitalized patients.

Material and Methods: It were included clinical studies indexed in Pubmed, Lilacs and Scielo databases from 2008 to 2017, following pre-determined inclusion and exclusion criteria. Results: twelve studies met the inclusion criteria and were reviewed. According to the quality of the evidence, three studies were evaluated as I, six as II and three as III. Regarding the treatment used, clinical researches investigating the effectiveness of different antimicrobial solutions for oral hygiene in order to reduce aspiration pneumonia in hospitalized patients. Different chlorhexidine concentrations (0.05%, 0.1%, 0.12%, 0.2%, 2%) were used, as well as other substances for mouthwash. Conclusion: the lack of high quality studies undermines the confidence on the effectiveness of antimicrobial solutions regarding the reduction of aspiration pneumonia. However, those studies with good methodology suggested the reduction of pneumonia by oral hygiene.

Keywords: Oral hygiene; Chlorhexidine; Aspiration pneumonia; Oral health; Intensive therapy.

Introduction
The aspiration of oral pathogens is a pathological mechanisms involved in pneumonia acquired in hospital (PAH) and it is associated with supine position, dysphagia, changes in mental status, esophageal motility disorders, vomiting, acid reflux, intubation enteral nutrition, tracheal intubation, oropharyngeal and bronchial colonization, tracheostomy and alcoholism.

In sick patients, the aspiration of substances from oropharyngeal or concentrated secretions above the cuff orotracheal tube is the primary means for inoculation, in the lower respiratory tract, of oral pathogens, from dental biofilm, periodontal disease and caries.

When the pathogens overcome defense mechanisms of the respiratory system, which can be mechanical (cough reflex, reflex and glottal mucociliary system), humoral (antibodies and complement system) and/or cellular (polymorphonuclear leukocytes, macrophages and lymphocytes), it can occur pneumonia. It should be emphasized that patients with change in level of consciousness, a common condition in intensive care units (ICU), often aspirate greater amounts of secretions from the mouth.

The aspiration pneumonia has been correlated to the plaque and oropharyngeal colonization in patients receiving mechanical ventilation (MV). The endotracheal tube acts as a conductor of the oropharyngeal microorganisms to the lower respiratory tract, and these are often identified as etiological agents of nosocomial pneumonia. This pneumonia can also be caused by foreign material originating in oral cavity, most commonly, scraps of food, saliva, biofilm or a combination of these.

In order to reduce nosocomial pneumonia and ventilator-associated pneumonia (VAP), it has been recommended topical use of chlorhexidine (chemical agent of broad spectrum) during the care of oral hygiene in patients.

A recent review showed that microorganisms of dental biofilm or associated with periodontal disease have been found in bronchoalveolar lavage samples from hospitalized patients, and that poor oral hygiene seems to be one of the most common risk factors for PAH. In edentulous individuals, oral pathogens may persist even after extraction of natural teeth; hence, tongue saburra was identified as a risk indicator for aspiration pneumonia.

Oral health care seem to play an important role in the prevention of aspiration pneumonia in weak elderly. However, it is not clear what intervention is more effective in reducing the risk of aspiration pneumonia. The objective of this study was to perform a critical review of clinical trials that investigated if mechanical or chemical oral hygiene can prevent aspiration pneumonia in hospitalized patients.

Material and Methods
This literature review was performed by using a search protocol prepared by the authors (NPGN and ODF), following the criteria of the Consolidated Standards of Reporting Trials (CONSORT): randomization, allocation concealment, blinding, losses in follow-up and sample size estimation. It was included clinical trials, randomized or not, conducted in sick hospitalized patients, in intensive care or in other sectors, regardless of sex, age and race. The intervention of interest was oral hygiene, without technical restrictions and the outcome was the prevention or reduc-
The research was conducted in Pubmed, Scielo and Lilacs databases, using the following key words in combination or not, in English and Portuguese: “oral hygiene, chlorhexidine, aspiration pneumonia, intensive care medicine, mechanical ventilation, biofilm, oral health”.

For quality assessment of the trials, a criterion was adapted from Ho et al., based on CONSORT and on the following criteria for the qualification of the methodology and classification of levels of evidence: randomization, allocation concealment, masking, losses in follow-up and sample size estimation (table 1).

A detailed evaluation of selected articles was conducted, and several items were taken into account in order to have a general notion for final evaluation. These items were: author/year, study design, sample size, objectives, criteria for inclusion, intervention, confounding factors and conclusion.

The final evaluation was made from the classification of each article according to the criteria selected. Each article was separated by table, for each assessment item. Later, they were put together in an only table for the classification of levels of evidence found.

Results

It were retrieved 91 articles. After application of the eligibility criteria, it were full read 13 manuscripts. Twelve studies were selected and included, they were published in English, from the year 2008 to 2017. One study was excluded for not presenting a conclusion about the effect of oral hygiene on the incidence of VAP. Figure 1 shows the flowchart of the studies for identification, inclusion, and qualitatively analysis.

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**Table 1. Classification for assessing the quality of clinical trials**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>Appropriate</td>
<td>Partially reported</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Randomization</td>
<td>Appropriate</td>
<td>Partially reported</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Appropriate</td>
<td>Partially reported</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Masking</td>
<td>Appropriate</td>
<td>Partially reported</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Losses</td>
<td>Appropriate</td>
<td>Partially reported</td>
<td>Not mentioned</td>
</tr>
</tbody>
</table>

Criterion adaptated from S. He et al. 2011 and Nogueira et al. 2015.

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**Figure 1. Flowchart of selection and inclusion of articles**
The Table 2 presents a summary of the 12 selected studies and the classification given in accordance with the levels of evidence. It is important to note the vast heterogeneity of the variables, and the samples have different sizes. There are several types of interventions used, as well as, the inclusion criteria.

### Table 2. Summary of selected studies

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Design</th>
<th>Sample</th>
<th>Objective</th>
<th>Inclusion criteria</th>
<th>Intervention</th>
<th>Confounding factors</th>
<th>Conclusion</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharif-Abdullah et al. 2016</td>
<td>Double-blinding, controlled, randomized, parallel</td>
<td>35 subjects &gt; 65 years</td>
<td>Effect of CHX 0.2% and thymol in hospitalized patients</td>
<td>Patients older than 65 years, no prosthesis</td>
<td>OH and CHX 0.2% in intervention group, and thymol in control group</td>
<td>NM</td>
<td>CHX 0.2% reduced oral colonization. Easy and economical OH</td>
<td>I</td>
</tr>
<tr>
<td>Scannapieco et al. 2009</td>
<td>Randomized, double-blinding</td>
<td>547 subjects &gt; 18 years</td>
<td>Frequency of CHX 0.12% in reducing respiratory pathogens</td>
<td>Purulent secretion, leukocytosis, chest X-ray</td>
<td>OH with CHX and MB, separated or combined</td>
<td>NM</td>
<td>CHX reduced viable amount of S. aureus, in ICU-MV. The CHX didn’t reduce total amount of PR.</td>
<td>I</td>
</tr>
<tr>
<td>Vidal et al. 2017</td>
<td>Randomized prospective</td>
<td>213 subjects &gt; 18 years</td>
<td>OH by MB with gel CHX 0.12% reduce VAP incidence</td>
<td>Fever, leukocytosis, chest X-ray, PRS</td>
<td>Yes: heart patients</td>
<td>Patients undergoing MB reduced duration on VAP</td>
<td>I</td>
<td></td>
</tr>
<tr>
<td>Nobahar et al. 2016</td>
<td>Randomized clinical trial</td>
<td>68 subjects &gt; 18 years</td>
<td>Effect of HP on the incidence of VAP</td>
<td>Patients under MV &gt; 48 hs, no IC for oral use, nor the head elevation 30°</td>
<td>HP group x placebo group with saline</td>
<td>Smoking and drug abuse</td>
<td>VAP reduction was more effective with HP</td>
<td>II</td>
</tr>
<tr>
<td>Azimi et al. 2016</td>
<td>Clinical study, randomized, double-blinded</td>
<td>39 subjects &gt; 15 years</td>
<td>Evaluate effects of 0.2% CHX, matriarch and SS</td>
<td>Patients with ET tube or NG, MV &gt; 48, no antibiotic treatment prior to hospitalization, no sensitivity to BA.</td>
<td>Mouthwash with CHX 0.12% in the control group and MB x CHX in the intervention group</td>
<td>NM</td>
<td>Mouthwash with CHX 0.2% reduces bacterial colonization</td>
<td>II</td>
</tr>
<tr>
<td>Hollaar et al. 2015</td>
<td>Randomized clinical trial, controlled, multi-center</td>
<td>500 subjects &gt; 65 years</td>
<td>Assess applica-tion of 0.05% CHX on VAP reduction</td>
<td>Disabled patients with symptoms of disfagias .</td>
<td>Application of 0.05% CHX</td>
<td>NM</td>
<td>Reducing the risk of developing pneumonia</td>
<td>II</td>
</tr>
<tr>
<td>Klarin et al. 2008</td>
<td>Randomized</td>
<td>50 subjects &gt; 18 years ou mais</td>
<td>Compare the pro biotic LP299 efficiency with CHX 0.1%</td>
<td>Chest x-ray, cultures AT occurring after 48 hours of MV</td>
<td>Oral MB followed by mouthwash with 0.1% CHX and application of emulsion of LP 299</td>
<td>NM</td>
<td>No differences were found between 0.1% CHX and LP299</td>
<td>II</td>
</tr>
<tr>
<td>Naiktari et al. 2014</td>
<td>Clinical study, multi-center, dou-ble-blinding, randomized.</td>
<td>120 subjects &gt; 20 a 65 years de idade</td>
<td>Compare effectiveness of mouthwash with trifala x 0.2% CHX</td>
<td>Hospitalized patients + plaque + calculus and clinical signs of IG.</td>
<td>Mouthwash with CHX, distilled water and trifala divided into groups.</td>
<td>NM</td>
<td>Trifala is effective as CHX 0.2%</td>
<td>II</td>
</tr>
<tr>
<td>Tantipong et al. 2008</td>
<td>Randomized</td>
<td>207 subjects &gt; 18 years ou mais</td>
<td>Efficacy of oral decontamination with 2% CHX or normal SS.</td>
<td>Temperature, leukocytosis, purulent aspiration</td>
<td>Oral decontamination with CHX 2% in a group and normal in other SS</td>
<td>NM</td>
<td>CHX 2% solution is an effective method in preventing VAP in patients receiving MV</td>
<td>II</td>
</tr>
</tbody>
</table>
The trials had evidence levels I, II, or III according to the rating scale for assessing the quality of randomized clinical trials. The twelve articles that fully or partly filled the inclusion criteria inclusion were randomized clinical trials, four presented allocation concealment, eight reported masking, two cited confounding factors, seven mentioned losses in follow-up. Seven studies explained the sample calculation. Only three clinical trials received evidence level I, six received II and three were rated III (table 3). Studies that was rated as level of evidence I, may be considered to have low risk of bias; those with evidence of level II, have moderate risk of bias; and the qualified as III, can carry high risk of bias.

Table 3. Methodological evaluation of included articles

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Sample size</th>
<th>Randomization</th>
<th>Allocation concealment</th>
<th>Masking</th>
<th>Losses</th>
<th>EL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scannapieco et al. 2009</td>
<td>YES=A</td>
<td>YES (computer=A)</td>
<td>YES=A</td>
<td>YES (TB=A)</td>
<td>YES=A</td>
<td>I</td>
</tr>
<tr>
<td>Vidal et al. 2017</td>
<td>NM=C</td>
<td>YES (envelope=A)</td>
<td>YES =A</td>
<td>YES (DB=A).</td>
<td>YES=A</td>
<td>I</td>
</tr>
<tr>
<td>Nobahar et al. 2016</td>
<td>NM=C</td>
<td>YES (coin=A)</td>
<td>YES=A</td>
<td>YES (DB=A)</td>
<td>NM=C</td>
<td>II</td>
</tr>
<tr>
<td>Azimi et al. 2016</td>
<td>YES=A</td>
<td>YES (NC=B)</td>
<td>NM=C</td>
<td>YES (DB=A)</td>
<td>NM=C</td>
<td>II</td>
</tr>
<tr>
<td>Hollaar et al. 2015</td>
<td>YES=A</td>
<td>YES (NC=B)</td>
<td>NM=C</td>
<td>NM=C</td>
<td>YES=A</td>
<td>II</td>
</tr>
<tr>
<td>Klarin et al. 2008</td>
<td>NM=C</td>
<td>YES (NC=B)</td>
<td>NM=C</td>
<td>YES (SB=A)</td>
<td>YES=A</td>
<td>II</td>
</tr>
<tr>
<td>Naiktari et al. 2014</td>
<td>YES=A</td>
<td>YES (NC=B)</td>
<td>NM=C</td>
<td>YES (SB=B)</td>
<td>YES=A</td>
<td>II</td>
</tr>
<tr>
<td>Tantipong et al. 2008</td>
<td>YES=A</td>
<td>YES (NC=B)</td>
<td>NM=C</td>
<td>NM=C</td>
<td>YES=A</td>
<td>II</td>
</tr>
<tr>
<td>Scannapieco et al. 2012</td>
<td>YES= A</td>
<td>YES (PB=A)</td>
<td>NM=C</td>
<td>NM=C</td>
<td>NM=C</td>
<td>III</td>
</tr>
<tr>
<td>Tuon et al. 2017</td>
<td>NM=C</td>
<td>YES (NC=B).</td>
<td>NM=C</td>
<td>NM=C</td>
<td>NM=C</td>
<td>III</td>
</tr>
<tr>
<td>Estaji et al. 2016</td>
<td>NM=C</td>
<td>YES (PB=A)</td>
<td>NM=C</td>
<td>YES (SB=B)</td>
<td>NM=C</td>
<td>III</td>
</tr>
</tbody>
</table>

PB = permuted block  
NC = Not clear  
SB= simple-blinding  
DB = double-blinding  
EL = evidence level  
NM = not mentioned  
TB = triple-blinding
Discussion

Studies have reported that oral hygiene in sick patients prevents infections and secondary diseases such as aspiration pneumonia. However, there are few clinical trials in the literature evaluating the effectiveness of oral hygiene in the prevention of this condition. The main prevention cited by the revised studies is the oral hygiene through mouthwash with antimicrobials and/or mechanical brushing.4-12,22

The studies of Vidal et al.,4 Sharif-Abdullah et al.12 and Scannapieco et al.13 had evidence level I and followed almost every criterion.8 A study4 did not report the sample calculation which is very important to determine the amount needed to compose the sample in order to obtain valid results, but, no more than enough.23 In the study of Vidal et al.,4 there was a significant reduction in the duration of mechanical ventilation and tendency to reduce the incidence of VAP and duration time of staying in the ICU, although this last result without statistic significance. The authors compared the tooth brushing with and without chlorhexidine 0.12%. The authors4 concluded that more studies would be needed to define the ideal oral hygiene, dental plaque index, which is important to evaluate before and after the intervention to compare its reduction in oral cavity and the effect of the intervention, the observation of the impact of measures of oral hygiene, mainly in the hospital mortality rates and ITU.

The studies of Sharif-Abdullah et al.12 and Scannapieco et al.13 had similar conclusions in reducing oral colonization by bacteria. The first one used chlorhexidine 0.2%,12 and the second one13 used chlorhexidine 0.12%. Both12,13 reported that the use of chlorhexidine reduced oral colonization. A study13 reported the reduction only of S. aureus and other12 stated positive effect in reducing oral colonization when compared with oral care routine.

All studies with level of evidence I4-12,13 reported losses in follow-up. When there are losses of contact with some participants, the researchers cannot complete the collection of data as planned.24 Studies can be affected by clearances, withdrawals and losses of participants, which could void the initial equivalence of the experimental and control groups. To manage these deviations, two strategies are commonly used: the principle of analysis by intention to treat (ITT) states that any person must be parsed as if he had followed completely the project programmed; and protocol analysis (per-protocol = PP) that proposes to include only those volunteers who joined the designated intervention and concluded the following default, without any deviation of the main protocol.10 Studies that reported losses, did not mention they were administered.

The studies of Nobahar et al.,14 Azimi et al.,15 Hollaar et al.,16 Klarin et al.,17 Naiktari et al.,18 and Tantipong et al.,19 had evidence level II. Only Nobahar et al.14 presented the allocation concealment, which is a method used to ensure that the random sequence of subjects selected for intervention/control groups is followed and kept hidden until the time of the intervention, thus avoiding, bias selection. This technique prevents the researchers, unconsciously or not, to determine in advance which participants will be allocated to a certain group.24

Clinical trials in which the sequence of allocation was improperly hidden can produce larger estimates of treatment effects than the tests in which the authors report adequate concealment. The conduct for the generation of sequence has a smaller role in preventing bias than the conduct for concealment. Having a random (unpredictable) sequence should make little difference without adequate concealment.10

Only the studies of Hollaar et al.16 and Tantipong et al.,19 among the classified as II, were masked. This is an important element in a clinical trial, because intentionally not knowing the treatment of each individual is receiving avoids subjectivities, bias and prejudices, which could introduce bias.25 However, regarding the randomization of the studies with evidence level II, the only one clear enough was the study of Nobahar et al.14 Randomization is a search strategy used to increase the validity of clinical trials that assess the effect of interventions.26

Two studies4,14 mentioned confounding factors that are able to influence both the dependent and independent variable. These factors (for example, baseline characteristics, prognostic factors or concomitant interventions) can generate bias in the estimated effect of intervention.24 Oral hygiene is a major preventive factor to parkinsonian which can be susceptible to aspiration and colonization of bacilli and bacteria that are the main responsible for the development and severity of aspiration pneumonia.27

The studies that had evidence level III were of poor quality, without enough data, unable to consider any evidence and at high risk of bias. Clinical trials compared or investigated the effectiveness of an antimicrobial for oral hygiene of patients, and their impact in the prevention of pneumonia. According to Amral et al.,28 in patients admitted to ICU, oral hygiene is usually precarious, also, there is reduced salivary flow by use of some drugs, which contributes to the increase of biofilm, and consequently its complexity, favoring the oral colonization by respiratory pathogens.

It is difficult to compare the studies due to the diversity of interventions and results for each test. Over the different chlorhexidine concentrations (2%, 0.12%, 0.05%, 0.2%, 0.1%), other substances were used for mouthwashes such as hydrogen peroxide, Thymol, matriarch, probiotic bacteria Lactobacillus plantarum 299, saline solution, and trifala.

The aspiration pneumonia was defined by most studies as acquired pneumonia after 48 hours in hospital stay post...
intubation for mechanical ventilation. The diagnosis was diversity in several studies and involved temperature, leukocytosis, chest x-rays, tracheal aspirates. And it pathogenesis is related to aspiration of bacteria from cavity and upper airway to the lungs due to low immunity of the host and biofilms that are reservoirs for microorganisms. The literature indicates oral health as an important factor in preventing and/or improving the patient’s systemic health, indicating that oral amendments can be considered hotbeds for systemic spread of pathogens, especially in patients with compromised health.\textsuperscript{29}

Articles with evidence level I or II presented a variety of objectives and conclusions, making it difficult to establish a comparison. There is no standardized methodology that allows it. Nevertheless, those that aimed to compare the reduction of pneumonia incidence or microbial reduction,\textsuperscript{12,14,16,18,19} didn’t present statistically significant conclusion that the oral hygiene can reduce the incidence of aspiration pneumonia, except the study of Vidalet et al.\textsuperscript{4} These results agree with a systematic review on oral hygiene and pneumonia in children in ICU\textsuperscript{31} which concluded that there is no scientific evidence to support the use of oral hygiene isolated with chlorhexidine to prevent PVA. Overall, there are no well-established protocols that aim the best method of oral hygiene for children admitted to ICU.

Many patients who are admitted to hospital present oral hygiene deficiency and oral problems such as caries, periodontal disease, calculus, which become focus of infection and can overcome the immunological defenses of the weak patient, achieving blood and reaching other organs. To prevent systemic infections of odontogenic origin, Dentistry comes changing history of curative treatments only for preventative care, looking at the patient as a whole and seeking the best quality of service, not only in offices, but extending to hospital environments.\textsuperscript{30}

Assuming oral microorganisms are involved in the origin of aspiration pneumonia, this question arises: if oral hygiene measures reduce the risk inherent of oral biofilm. Whereas mechanical hygiene measures appear to reduce the incidence of pneumonia, the use of chemical agents alone yielded little improvement in the incidence of upper respiratory tract infections.\textsuperscript{31} It is recommend tooth brushing after every meal, cleaning removable dentures once a day and professional oral health care once a week as the best scheme to reduce the incidence of aspiration pneumonia.\textsuperscript{7} The reviewed studies,\textsuperscript{4,12,22} presented reduced oral colonization through oral hygiene with mouthwash and mechanical brushing, emphasizing the study of Estaji et al.,\textsuperscript{22} that reported remarkable impact using toothbrush in reducing oral lesions.

An important finding of this review showed that appropriate oral health care decreased the amount of potential respiratory pathogens, and suggested a reduction in the risk of aspiration pneumonia, consequently, an improvement in the reflection of swallowing and cough reflex sensitivity. However, it still remains the question of what is the most effective intervention in reducing the incidence of aspiration pneumonia in the elderly. An individualized approach based on the assessment of the risk of aspiration pneumonia may be the best guide to determine the content of a program for prevention of oral health more intensive.\textsuperscript{7}

Studies with humans are limited by ethical questions that respect and protected the health of the participants. Some groups of people are considered vulnerable, and need special attention, for example, the hospitalized patients. These patients often cannot give or refuse consent for themselves, due to the situation in which they are.\textsuperscript{29} Therefore, the few researches in sick patients, often due to the low availability due to vulnerability of patients and the priorities of family and health professionals engaged in the rehabilitation of the health and comfort of patients.

Another important aspect to be addressed herein are the hospital costs of nosocomial infections. The time of hospitalization can be increased by up to nine days because of nosocomial pneumonia, raising costs up to $40000, summing more than U $1.2 billion/year for the health system of the United States.\textsuperscript{32} Thus, the aspiration pneumonia impact both the patient’s health, worsening their condition and may lead to death, and, every institution, increasing the length of stay of patients and consequently the hospital costs.

This review was limited due to low methodological quality of the included studies. The strong point of the review was detailed and critical evaluation of the items considered important to a good level of evidence of clinical trials included. There is a need for further studies to be carried out with a good methodological quality, containing more foundations and scientific evidence on the subject. It is important to have a clarification on the subject, which could lead to hospitals, nursing homes and homes for the elderly to control hospital infection and reduce to the number of deaths by secondary infections, with professional interaction between doctors, dentists and health officers in these institutions.

**Conclusion**

In this study, it could be concluded that there are need for more studies to ensure evidence that antimicrobial solutions can reduce the aspiration pneumonia, however, studies with good levels of evidence suggest that this may happen with the oral hygiene care, which brings benefits to the patient and every institution, by reducing the mortality rate and the hospital costs. Also, it is important dentists stay in the hospital, promoting professional interaction and a better quality of life to the patient.
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References

Mini Curriculum and Author’s Contribution
2. Patricia Furtado Gonçalves – DDS and PhD. Contribution: co-advisor, conception and design, data acquisition, writing the work.
3. Dhelfeson Willya Douglas-de-Oliveira – DDS and MSc. Contribution: methodological review of the article, data acquisition, formatting tables and responsible for submission.
4. Olga Dumont Flecha – DDS and PhD. Contribution: Advisor, data acquisition and interpretation, writing work, final approve.

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