

## COMMENTS TO RESEARCH ARTICLES

### Effects of chlorhexidine gluconate oral care on hospital mortality: A hospital-wide, observational cohort study<sup>☆</sup>

#### Los cuidados con clorhexidina bucal en la prevención de la neumonía asociada a ventilación mecánica a debate

Deschepper M, Waegeman W, Eeckloo K, Vogelers D, Blot S. Effects of chlorhexidine gluconate oral care on hospital mortality: a hospital-wide, observational cohort study. *Intensive Care Medicine*. 2018;44(7):1017-1026.

#### Resumen

#### Purpose

Chlorhexidine oral care is widely used in critically and non-critically ill hospitalized patients to maintain oral health. We investigated the effect of chlorhexidine oral care on mortality in a general hospitalized population.

#### Methods

In this single-center, retrospective, hospital-wide, observational cohort study we included adult hospitalized patients (2012-2014). Mortality associated with chlorhexidine oral care was assessed by logistic regression analysis. A threshold cumulative dose of 300 mg served as a dichotomic proxy for chlorhexidine exposure. We adjusted for demographics, diagnostic category, and risk of mortality expressed in four categories (minor, moderate, major, and extreme).

#### Results

The study cohort included 82,274 patients of which 11,133 (14%) received chlorhexidine oral care. Low-level exposure to chlorhexidine oral care ( $\leq 300$  mg) was associated with increased risk of death [odds ratio (OR) 2.61; 95% confidence interval (CI) 2.32-2.92]. This association was stronger among patients with a lower risk of death: OR 5.50 (95% CI 4.51-6.71) with minor/moderate risk, OR 2.33 (95% CI 1.96-2.78) with a major risk, and a not significant OR 1.13 (95% CI 0.90-1.41) with an extreme risk of mortality. Similar observations were made for high-level exposure ( $> 300$  mg). No harmful effect was observed in ventilated and non-ventilated ICU patients. Increased risk of death was observed in patients who did not receive mechanical ventilation and were not admitted to ICUs. The adjusted number of patients needed to be exposed to result in one additional fatality case was 47.1 (95% CI 45.2-49.1).

#### Conclusions

These data argue against the indiscriminate widespread use of chlorhexidine oral care in hospitalized patients, in the absence of proven benefit in specific populations.

Critical reading was undertaken following the model of the Spanish Critical Appraisal Skills Programme (CASPE):

#### Comments

Mechanical ventilator-associated pneumonia is a severe, largely avoidable, adverse effect in critically ill patients. The main preventive strategies include promoting safe practices, improving aspects such as delayed extubation, minimising subglottic and oropharyngeal microaspiration, and using oral chlorhexidine as an antiseptic in different concentrations to modulate oropharyngeal colonisation.<sup>1</sup>

This procedure has been widely studied in the literature; the use of high concentrations of chlorhexidine achieves

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a significant reduction in the risk of ventilator-associated pneumonia in patients who have undergone heart surgery.<sup>2</sup>

These studies have helped make oral care with chlorhexidine an essential part of the preventive measures against ventilator-associated pneumonia for intubated patients and, by default, for all patients admitted to health centres.

Although cases of severe adverse effects associated with the use of chlorhexidine have been published, they refer to occasional episodes, failing to adhere to the recommended concentrations and allergic reactions.<sup>3</sup>

A meta-analysis by Klompas<sup>4</sup> that included 3630 patients and aimed to assess the effect of oral care with chlorhexidine in the prevention of ventilator-associated pneumonia found expected information concordant with other already published data, on how the use of chlorhexidine reduces the risk of pneumonia in patients who have undergone heart surgery, but this data was not significant for other ventilated patients. However, they also found unexpected, paradoxical data; they observed a greater risk of death in patients who had not undergone heart surgery who had received oral care with chlorhexidine. This and other similar studies<sup>5</sup> have raised doubts as to the benefits of generalising oral care with chlorhexidine, and as to its safety. It was at this point that this study was designed with a large cohort of all types of hospitalised patients to evaluate the effect of oral care with chlorhexidine on mortality.

## Assessment of results

The study revealed that oral care with chlorhexidine is associated with a greater risk of mortality and, in turn, this greater risk is associated with more favourable prognoses, and no effect was found in patients subjected to mechanical ventilation or heart surgery, which contradicts the conclusions of previous studies that found a protective effect of oral care with chlorhexidine in these types of patients specifically. The main problems in accepting the results obtained concern the characteristics of the study itself, and the extensive and diverse population it analyses. The analysis covers all the centre's adult patients, irrespective of their condition, level of dependency for care and treatment, grouping them into diagnoses according to administrative criteria, which makes it difficult to classify the real prognosis, especially when the end objective is to associate mortality with an uncontrolled care procedure.

In the development of the analysis mortality was not correlated with variables such as dose administered or the intensity of care from health staff, obtaining surprising data, such as an unexpectedly high crude mortality rate in the few patients not admitted to ICU receiving oral care with chlorhexidine. Therefore it is impossible to accurately establish possible effects of continuous exposure to chlorhexidine according to the dose used and the frequency of the procedure.

Despite the methodological problems inherent to a retrospective, single-centre, observational study, with many

confusion and bias factors, and despite obtaining paradoxical results that are difficult to justify, uncertainties have been raised that require the generalised use of chlorhexidine for the oral care of all patients to be reconsidered. Further studies that are correctly designed are needed with the clear aim of specifically analysing the population of critical and ventilated patients, and that provide the necessary evidence to ensure the safety of these preventive actions. It is essential to clarify any potential risks and benefits, the most effective non-toxic levels, and the most suitable way of using this procedure.

It is urgent that the scientific community generate this evidence when concerns are raised about recommendations that are widespread and entrenched in daily practice in our intensive care units, particularly for critical, ventilated patients.<sup>6</sup>

Prudently, and pending scientific evidence that provides robustness to and endorses new changes to this preventive strategy, the Advisory Committee of the Ministry of Health and the Consumer, for Safety Projects for Critical Patients have amended the grade of this recommendation from obligatory to recommended.

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