CLINICA DELLE MALATTIE INFETTIVE
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STUDY PROTOCOL

Study on the Effect of the Universal Decontamination with daily bathing with 4% Chlorhexidin gloconate on the Incidence of Hospital Acquired Infections in Intensive Care Units.

Study code

DUCLOREXINT

Version 1, April 27th, 2015

Table of contents

Introduction

All hospital-acquired infections (HAI) and especially, HAI due to multi-drug resistant (MDR) micro-organisms are, nowadays, one of the most relevant matter of concern because of their clinical and economic consequences [1-2].
Several infection control measures (sistematic careful hand hygiene, selective and universal decontamination, etc…) have been investigated for their effect on HAI acquisition rate [3-6]. Chlorhexidine gluconate-based universal decontamination appear to be a promising strategy [8], but other studies didn't support these findings [8].

Aims of the study

Main aim:
Evaluation of the effect of daily bathing with 4% chlorhexidine gluconate (CHG)-containing soap on the incidence of HAI in 2 intensive care units.

Secondary aim:
Evaluation, if possible, of the effect of daily bathing with 4% CHG-containing soap on the incidence of possible and probable ventilator-associated pneumonia (VAP), bloodstream infection (BSI), central-line associated bloodstream infections (CLABSI), urinary tract infections (UTI) and catheter-associated urinary tract infections (CAUTI).

Definitions and methods:

Demographic characteristics and clinical data of patients will be collected using a case report form that was elaborated specifically for this study (attachment 1) .
Definitions
We will take into consideration only the infections arisen at least 48 hours after the admission to the above mentioned wards.
Sepsis is defined as a systemic inflammatory response syndrome (SIRS) with a probable and/or confirmed infection [9].
Specifically, VAP, BSI, CABSI, UTI e CAUTI are defined according to the National Healthcare Safety Network – Centers for Diseases Control and Prevention definitions [10].

Study design

Prospective single-blinded randomized case-control study.

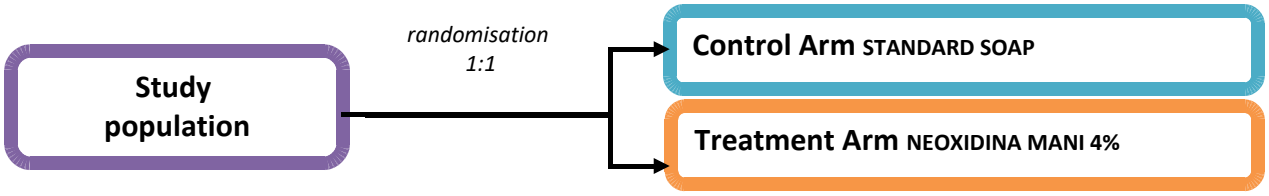
Study population: all patients admitted to the Intensive Care Unit (ICU) or to the Post-Cardiosurgical Intensive Care Unit (PC-ICU) of the University Hospital of Perugia will be enrolled.
These patients will be randomized in two arms using a specific software. Patients in the first arm (control arm) will undergo the usual hygiene procedures with standard soap; in the second arm (treatment arm) patients will be bathed with 4% CHG-containing soap (Neoxidina mani 4%), at least 30 ml according to the manufacturer indications (see the attached data sheet). In particular the whole body surface – except for the face – will be i) humidified

with water impregnated washcloths, ii) bathed with 4% CHG-impregnated washcloths (at least 30 ml) and, after at least 30 seconds, iii) rinsed with water-impregnated washcloths.
This product is already in use in our hospital to prepare patients before a surgical intervention. We will evaluate and compare the global insidence of sepsis in the two arms and, secondary, incidence of VAP, BSI, CABSI, UTI and CAUTI.

In addition to this, we will collect demographic data of each patients and data about comorbidities, cause of admission and infections occured during the hospital stay.

This study is single-blindend. Physicians that have to collect data, to diagnose infections and to analyse data won't be directly involved in washing procedures and they are not member of the medical staff of ICU and/or TIPOC. Moreover, only nurses that will wash patients by their own hands will know the arm in which the patient is. Both the usual soap and the Neoxidina mani 4% (with chlorhexidine gloconate 4%) have no colour nor other item than can favour their identification.

Figure 1: Study design



Patients enrolment.
Inclusion criteria: all patients aged ≥ 18 years old admitted to ICU or TIPOC.

Exclusion criteria:
- Age < 18 years old;
- patients with burns;
- patients with known allergy to chlorhexidine and/or one of the components of Neoxidina mani 4%;
- patients with toxic epidermal necrolysis o Stevens-Johnson syndrome.
- pregnancy

Data will be collected on specific paper form and, then, analyzed using computerized methods (section "Criteria and data collection methods").

Relative risk of the procedure and risk/benefit evaluation.
Neoxidina mani 4% can rarely cause irritation of the exposed surfaces especially after prolonged exposure. To our knowledge, major adverse events due to Neoxidina mani 4% haven't been described till today.

Being randomised to the treatment arm could have a beneficial effect in term of hospital acquired risk reduction.
The aim of the present study is to evaluate if 4% CHG daily bathing in intensive care settings could reduce HAI acquisition rate. As a consequence, considering HAI-associated morbidity mortality and social costs [1-2], benefits appear to be higher than risks.

Sample Size
Sample size will be between 420 and 1000 patients. Sample size was calculated after a pre-trial evaluation of HAI. We retrospectively measured the pre-trial incidence of HAI at ICU and PC-ICU (patients admitted to ICU and PC-ICU between January, 1st and January, 31st 2015). Twenty patients out of 66 suffered from at least 1 HAI (incidence 30.3%).
By adopting an alpha error tolerance (false-positive risk) equal to 0.05, beta error tolerance (false-negative risk) equal to 0.1, power equal to 0.9, a potential reduction of HAI incidence by 10% and a percentage between 5% and 8% of potential dropouts, we calculated that a sample size of at least 410-420 patients would be required to provide sufficient power to detect significant differences.
According to the Italian Law, patients with altered mentation at the admission could be directly enrolled by the physician after a clinical evaluation. At the recovery of consciousness, the patient will receive the specific paper to provide his consent or not.

Data analysis
Data will be analysed with a statistical software. Distribution of variables will be assessed by Kologorov-Smirnov deviation. Normal variables will be represented as mean +/- standard deviation, continuous non Gaussian variables will be represented as median and interquartile range, categorical variables will be represented as frequency and percentage. Comparison between groups will be performed with two-tailed t-test, Mann-Whitney test or chi-square test with Yate's correction, depensind on variable distribution. Data analysis will be made by physicians blinded to the study arm.

Data collection.
We will enrol 420 to 1000 patients in up to one year. Ramdomisation will be done by a specific sofware; it will be a simple 1:1 randomisation at patient-level. To evaluate infections we will use data from the routine clinical practice; patients in the two arms will be evaluated in the standard way and without differences between the two arms.
Data will be collected with an ad hoc clinical report form (CRF); data about sex, age, demographic characteristics, comorbidities – evaluated by Charlson comorbidity index – and infections will be collected in the same above mentioned CRF.
These data will be collected and analysed by physicians blinded to the randomisation.

Patient's consent

Patients will be informed about the study protocol by an ad hoc chart with which they can provide their consent. For unconscious patients or patients unable to provide their consent, at admission a physician will decide patients' enrolment on the basis of their clinical conditions. These patients will provide their consent as soon as their regain consciousness.

Results publications

The findings of the present study will be published- if possible – on international medical journals. All the participating physicians will be citated according to their role in the study. All of them have copyright about these data.

Ethical considerations

The present study will be conducted to improve the present clinical practise and to reduce the risk of infection during the hospital stay. The proposed strategy appear to be promising to reach the declared aims and almost adverse event free fot patients. The present study will be conducted in agreement with the declaration of Helsinki.

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