Determination of tobramycin serum concentrations in ICU patients treated with SDD: a prospective study.

Published: 28-01-2016
Last updated: 15-05-2024

The purpose of this study is to provide insight in to what extent clinically significant systemic absorption of tobramycin occurs (resulting in a serum tobramycin concentration> 1.0 mg / L) in ICU and Medium Care ICU patients who are being...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON43386

Source
ToetsingOnline

Brief title
Tobramycin absorption is SDD users.

Condition

- Other condition
- Bacterial infectious disorders

Synonym
SDD, tobramycine absorption

Health condition

profylaxe optreden infecties

Research involving
Human

Sponsors and support

Primary sponsor: Martini Ziekenhuis
Source(s) of monetary or material Support: geld verkregen uit het geven van lezing. Dlt geld is in een onderzoekspotje van de rve farmacie bewaard tbv onderzoek.

Intervention

Keyword: Absorption, ICU patients, SDD, Tobramycin

Outcome measures

Primary outcome

The primary endpoint of this study is the achievement of a high (> 1.0 mg / L)

tobramycin serum concentration during the use of SDD.

Secondary outcome

Secondary endpoints of the study are:

Identification of risk factors that contribute to high systemic serum

tobramycin concentrations. To this end, we extract data from the patient record

in soft chip. With the data extraction the criteria of the National Intensive

Care Evaluation (NICE) will be used as much as possible.

Study description

Background summary

Selective decontamination of the digestive tract (SDD) has as main objective to reduce the risk of nosocomial pneumonia and candidaemie. In addition, an increase in antibiotic resistance is prevented by reducing the use of antibiotics for these infections. By eliminating aerobic potentially pathogenic micro-organisms (PPM), and yeasts from the gastrointestinal tract and oropharnyx the pharynx becomes no longer colonized with PPM and the risk of a nosocomial pneumonia caused by micro-aspiration is dereased. By early elimination of yeast in the digestive tract a general colonization (respiratory tract, wounds, urinary tract) is contested and thus decreases the risk of candidaemie. Within the Martini hospital all the patients admitted to the ICU

and Medium Care ICU with an expected duration of> 72 hours and / or expected duration of ventilation for> 48 hours will get treatment with SDD.

The SDD protocol consists of a combination of colistin / polymyxin E, tobramycin, and amphotericin B which is applied in the oral cavity in ventilated patients in a 2% concentration in Orabase paste, and is applied in the gastrointestinal tract by means of a suspension with the same antibiotics via the gastric tube. In patients that are not ventilated the mouth is rinsed with the suspension and then swallowed. This decontaminates the entire digestive tract (if intact). Furthermore, a short intravenous antibiotic therapy is given during the first four days, in order to treat or prevent emerging primary endogenous infections. The short intravenous antibiotic treatment is given only if there aren't any other antibiotics already given for other reasons.

It is stated that tobramycin is not absorbed after oral administration, making systemic tobramycin serum concentrations not expected. Detectable tobramycin serum concentrations (> 0.05 mg / L), however, have been reported in patients receiving SDD and are related to a decreased intestinal barrier in sepsis, shock or after major abdominal surgery. Renal impairment is associated with decreased systemic clearance of tobramycin and can thus lead to persistent high serum concentrations and / or accumulation of systemic tobramycin. To date, there is in the Martini Hospital currently no policy with regard to the determination of serum tobramycin concentrations in patients with an increased risk of systemic absorption of tobramycin. Determination of serum tobramycin concentration only occurs in patients with an increased risk of reduced elimination of tobramycin, so patients undergoing CVVH, who are (intermittently) dialyzed or have a eGFR <30 ml / min (in accordance with SWAB directive). There is also in the Martini hospital (rural) no clear policy on how to proceed with proven high tobramycin serum concentrations.

Recently, we have found high serum tobramycin concentrations (> 2 mg / L) in an ICU patient treated with SDD . Because this patient was not treated with systemic tobramycin it can be concluded that there has been absorption of tobramycin from the SDD. This patient had several risk factors for increased absorption and decreased elimination of tobramycin. The persistent SIRS, sepsis, renal dysfunction, major abdominal surgery and multiple administration routes of SDD (mouth paste, suspension and suppository) may have all contributed to the high systemic tobramycin serum concentrations.

From the systemic useof tobramycin it is known that the height of the trough serum concentration is a measure for the probability of the occurrence of nephrotoxicity. In the SWAB TDM monograph tobramycin, which is focused on IV administration of tobramycin, it is stated that when a trough serum concentration higher than 2 mg / L, tobramycin dosage should be adjusted. At a serum tobramycin concentration between 1 and 2 mg / L dose optimization is possibly necessary. So it is plausible that patients who have high tobramycin

serum concentrations (> 2 mg / L) due to SDD, have an increased risk for the occurrence of nephrotoxicity and ototoxicity.

Study objective

The purpose of this study is to provide insight in to what extent clinically significant systemic absorption of tobramycin occurs (resulting in a serum tobramycin concentration> 1.0 mg / L) in ICU and Medium Care ICU patients who are being treated with the SDD.
In addition, the goal of this research is to gain insight into risk factors that may contribute to an increased risk of absorption of tobramycin in the use of SDD.

Study design

The study is an observational cohort study. The cohort consists of all ICU patients and Medium Care ICU patients treated between February 1, 2016 and december 31, 2016 with SDD. In this group of patients a serum tobramycin concentration will be determined up to four times, using a immunoassay from Roche, the method of analysis which is currently being used for this. This serum is obtained by taking an additional tube of blood from the artery line, during the standard blood collection round at 6.00 am.

Study burden and risks

Withdrawal of blood from the artery line is an act that is performed several times daily in the ICU. It's standard procedure that each patient gets an artery at admission to the ICU because the ICU patient is by definition a critically ill patient. The IC staff is very competent in carrying out such actions. Therefore, there are no additional risks associated with this research.
The burden for patients is low, since blood will be collected not more than four times from an artery line for the purpose of this investigation. At admission at the ICU each patient standardly gets an artery line (= medical policy) and also, blood is taken from every IC patient daily at 6:00 am. In this study only once a week an extra tube of blood is drawn from the already existing artery. The patient does not need an extra injection for this study. High tobramycin serum concentrations increase a risk for renal dysfunction among other things. It is important, therefore, that high serum tobramycin concentrations are detected at an early stage. The results from this study are therefore important for future medical practice. For the reason above, this research is justified in the light of burdens and / or risks for the patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Signed informed consent
- Patient has to lie on the ICU or Medium Care - ICU
- Patient has to use SDD

Exclusion criteria

- Patients that are admitted to the burns IC
- Patients concurrently or within 72 hours prior to SDD treatment receiving tobramycin administered parenterally or pulmonary
- Patients who aren't treated with the regular schedule

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2016
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	28-01-2016
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	25-10-2016
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24557
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL55838.099.15
OMON	NL-OMON24557

Study results

Date completed:	23-11-2016
Actual enrolment:	50