Reduction of surgical-site infection in hip and knee arthroplasty: the influence of perioperative mupirocin nasal ointment and chlorhexidine soap in a double-blind, randomized, multicentre, placebo-controlled study.

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The purpose of this study is to determine whether it is useful to decolonize patients undergoing primary hip or knee replacement surgery from the S. aureus skin bacteria.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON41616

Source
ToetsingOnline

Brief title
**-trial

Condition

- Bacterial infectious disorders
- Joint disorders
- Bone and joint therapeutic procedures

Synonym
surgical site infections

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken
Source(s) of monetary or material Support: Achmea (SAG) Zwols wetenschap fonds;Isala klinieken. I&W fonds Isala klinieken

Intervention

Keyword: Arthroplasty, chlorhexidine digluconate, Infection, Mupirocin

Outcome measures

Primary outcome

primary we will look at wound infections, one years postoperatively, especially

with the S. aureus bacteria as the causative agent

Secondary outcome

secundary we will look at other micro-organisms responsible for postoperative

wound infections two years after surgery

Study description

Background summary

A primary infection after hip or knee prosthetics is one of the most feared complication. There are two types of infections; superficial and deep.
The definitions according to PREZIES being talked about;
Superficial infections:
- On skin or subcutaneous tissue occur within 30 days after surgery
- There is septic effusion in the incision or pain / localized swelling / redness / heat + positive wound culture or pain or tenderness / localized swelling / redness, heat and open surgical wound culture is positive or not cultured
Deep infections:
- Infection on deep tissue (fascia or muscle) occur within 1 year after surgery
- There is septic effusion from the deep incision or abscess or other sign of infection in observation / reoperation or at least one of the following

clinical symptoms (pain, swelling, redness, warmth, fever> 38 and spontaneous or surgically opened wound dehiscence and

Within Isala, the average infection rate (+ deeply superficial) over the period 2004-2012 for total hip arthroplasty os (THA) 3.32%, total knee arhtroplasties (TKA) are infected in 1.98% of cases. When we focus on the deep infections then 3.25% of primary total hip and 1.87% of primary total knee become infected. Nationwide, the percentage in the last 10 years is significantly lower, in 1.97 of hip replacement an infection is recorded. In 1.07% of cases there is a deep infection.
Of the total knee prosthesis 1.4% (superficial + deep) of patients is diagnosed as an surgical side infection, 0.83% is recorded as deep.

In this study we only focus on deep wound infections, because this patient group should be treated with, surgical dibridement and long-term intravenous antibiotics. Iff infection persists despite of antibiotic treatment and re-operation. Then should the prosthesis be removed. This prosthesis infection treatment is associated with high morbidity and costs. For the revision surgeries is this a factor of 4 higher. This revision is so heterogeneous group with respect to the variability in surgeries that it will not fall within the rationale of this study.
This prosthesis infection is slightly more than 50% of the cases Staphylococcus aureus (S. aureus), the causative agent, this percentage is also found in the UK and US hospitals (1, 2).
More than 80% (5-7) of the post-operative S. aureus infections are taken from the patient himself. Kalmus concluded that colonization with S. aureus causes an increased risk of infection in orthopedic patient population (8). It is therefore important to have free the patient pre-operative S. aureus. Mupirocin containing ointment intranasally eradiceert S. aureus carriers, and is proved to be effective for the prevention of wound infection in a case control study (9). However, in a pair of RCT's is no decline in the number of infections demonstrated within an orthopedic and general surgical patient population (10; 11). After a sub-analysis of the data showed that patients who were carrying S. aureus, mupirocin nasal ointment or effective (10; 11). Slover concluded that screening and perioperative eradication of S. aureus within the orthopedic patient population is cost effective (12). Recently there has been in the BMJ meta-analysis of 17 articles were published (13), it emerged the perioperative eradication provides a reduction of wound infections in patients undergoing orthopedic and cardiothoracic surgery. They also conclude that perioperative treatment with mupirocin nasal ointment (Bactroban®) and chlorhexidine-containing soap (Hibiscrub®) also gives a clear reduction in S. aureus-related wound infections. In the discussion, it is stated that it is heterogeneous groups of patients and therefore the results should be interpreted with caution.
About one third of the Dutch population is colonized with S. aureus. In addition, a portion varying colonized (30-60%) (9; 14-17), these patients can therefore be missed by pre-operative screening for S. aureus. A preoperative

real-time polymerase-chain-reaction (PCR) on S. aureus is logistics vulnerable and expensive.
Within cardiothoracic surgery Isala has over 10 years experience with the prophylactic use of Bactroban® nasal ointment without neglecting the development of resistance is seen. In addition, it is of course true that resistance development using Bactroban® nasal ointment in patients Non carrier is not at issue, because these patients no S. aureus carry, and this de facto can not be resistant.
After 5 days Bactroban® use about 91% nasal carriage is suppressed and there is no resistance seen (14). S. aureus may colonize at other locations such as underarms and perineum (18). For S. aureus in these locations to eradicating, use is made of chlorhexidine-containing soap (19). A similar scheme is used for eradication of methicillin resistant S. aureus carriers. Within Isala are placed annually 700 primary THA and TKA 400. If we add to this 12 hospitals it is expected that we at least annually 6,000 prostheses can be included. To determine the effectiveness of the eradication scheme will patients from Isala and Rijnstate Hospital enrolled themselves cultivate prior to eradication treatment of the pharynx, reduced both nostrils and perineum; these cultures will be repeated in the operating room. In retrospect, the nasal carriage and colonization of the preferred locations will be determined. In other words, it can be established with this, or this prophylactic treatment is effective.

Definition infection
The Center for Disease Control and Prevention (CDC) classifies a surgical wound infected when there is purulent discharge, positive cultures for microorganisms, wound dehiscence and the presence of sign Celsius (rubor, calor, dolor and tumor).
There are various systems score devised of which the asepsis score possible is the best example (20). This score makes it possible to differentiate between a minimum / superficial infection and often life-threatening deep infection (21).

Study objective

The purpose of this study is to determine whether it is useful to decolonize patients undergoing primary hip or knee replacement surgery from the S. aureus skin bacteria.

Study design

This double-blind randomized placebo-controlled study involved two groups

Group 1: starting six days before surgery with mupirocine nasal ointment two times each day each nostril until two days postoperatively.
This group also starts six days before surgery with Hibiscrub 4% soap solution until the day of surgery to decolonize the axillary and perineal region.

Group 2: starting six days before surgery with placebo nasal ointment two times each day each nostril until two days postoperatively.
This group also starts six days before surgery with placebo soap solution until the day of surgery to decolonize the axillary and perineal region.

When we decide at the oupatient clinc to place a primary knee or hip replacement, and informed consent is obtained. The patients enroll the study, Then we randomize the patients in one of both groups as discribed above. They will receive a bottle of soap and a tube of ointment with clear instructions

Intervention

Each included patient will start six days before surgery with mupirocin/placebo nasal ointment two times each day each nostril. He or she continues the ointment two days postoperatively.
Beside the nasal ointment they will also starts six days before surgery with chlorhexidine/placebo soap solution to decolonize the axillary and perineal region.. The soap is stopped at admission.

Study burden and risks

There is less risk for the participants of this study. The total duration covers seven days in which the participant use shampoo and nasal ointment. As described in the protocol, there are almost no side effects for the study medication, the only thing that can occur is local skin irritation, development of resistance is never seen in our thoracic surgery population.

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

All competent patients undergoing primary hip or knee replacement surgery

Exclusion criteria

non competent patiens
allergy to one of the products
major surgery at ipsilateral side in the past
already enrolled

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12000
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Chlorhexidine digluconate soap 40mg/ml
Generic name:	Chlorhexidine digluconate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Mupirocine nasal ointment 2%
Generic name:	Mupirocin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-11-2015
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-11-2015
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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: 20376
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2010-022701-17-NL
CCMO	NL32100.075.11
OMON	NL-OMON20376