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Original research article

Polihexanide for prevention of Wound Infection in Surgery. Is the contact time essential? POLIS-trial: A historic controlled, clinical pilot trial

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ABSTRACT

Background: The intraoperative irrigation of the surgical site with antiseptics in abdominal surgery has been previously proposed as a way to reduce the rate of surgical site infections. Polihexanide achieves the best results *in vitro*. We hypothesized that the application of this antiseptic to the surgical site throughout the whole surgical procedure is superior to its common use solely at the end of surgery.
Methods: In this pilot trial, we compared the long and short intraoperative application of polihexanide in elective abdominal surgery. In the "long" group, the subcutaneous tissue of the incisional wound was kept in contact with 0.04% polihexanide throughout the procedure. In the "short" group, wounds were merely irrigated with polihexanide immediately prior to skin closure.
Results: Forty-eight patients in the "long" group and 49 in the "short" group could be analysed. Surgical site infections occurred in 18.8% of the "long" and 20.4% of the "short" group patients. The adjusted infection rates were 19.8% and 16.1%, respectively.
Conclusions: Crude and adjusted SSI rates of both groups were nearly similar, so we concluded that this pilot data showed no measurable difference and a trial with larger sample size would be needed to determine a difference.

1. Background

Superficial and deep surgical site infections (SSI) are common postoperative complications of abdominal surgery. Despite improvements in surgical methodology, the development of new antibiotics, and an increased knowledge of the pathophysiology of chronic wounds, SSI are still the most common nosocomial infections [1]. Infection rates up to 26% are reported in individual studies [2]. SSI leads to a substantial morbidity and potential for mortality. Besides a prolonged hospital stay, a significant financial burden can result from these complications [3,4].

Since the middle of the 19th century, surgical wounds have been flushed with antibacterial solutions by Lister and others [5] to create antiseptic conditions. This led to significant reductions in mortality rates. However, because of the severe side effects of the components of the antibacterial solutions, a search for suitable antiseptic substances began [6]. The discovery of antibiotics led to the abandonment of a further search. In the current era of rising bacterial resistance to antibiotics, there is an increased interest in wound antisepsis.

Cleansing the wound prior to skin closure has been found to reduce the rate of SSI when used in addition to routine systemic antibiotic prophylaxis [7–9]. The topical application of antiseptics reduces the bacterial contamination of the subcutaneous tissue [10]. By this measure, the number of colony-forming units could be reduced to levels below the relevant threshold for infection. The advantages of polihexanide over other antiseptics can be shown *in vitro* [11]. An interaction with systemic antibiotics has also been demonstrated *in vitro*. In contrast to chlorhexidine, a synergistic effect for polihexanide was demonstrated [12].

Numerous scientific publications discuss the application of polihexanide on chronic wounds, where safety has been sufficiently demonstrated. Anaphylactic reactions to polihexanide have been rarely described despite its widespread use in cosmetics [13]. It is therefore assumed that a minimal risk of allergic reaction exists [14].

The largest study to treat wounds with polihexanide was performed on over 7800 patients with contaminated traumatic wounds, and was able to demonstrate a significant reduction in wound infection risk [15]. The application of polihexanide to

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contaminated traumatic wounds is therefore recommended. The efficacy of polihexanide has been demonstrated against both gram-positive and gram-negative bacteria [16,17].

Previous meta-analyses demonstrated that intraoperative wound irrigation in abdominal surgery reduces wound complications [18,19]. However, no studies evaluating the intraoperative application of polihexanide exist, despite *in vitro* data suggesting that polihexanide is more effective than povidone-iodine [11]. One randomized trial evaluating the prevention of wound infections from catheter exit-sites showed a clear benefit of polihexanide over saline and povidone-iodine [20]. Actually one large trial is ongoing to prove the superiority of polihexanide over saline lavage (DRKS00002698).

Polihexanide has a slow onset of action, and microorganisms have different sensitivities to it depending upon the exposure time. Therefore, wound contact with polihexanide for 10–15 min is required [21]. Polihexanide was shown to inhibit microbial attachment to wound surfaces through an interaction with the bacterial membrane [22]. Furthermore, the early lavage of wounds with polihexanide has been demonstrated to be more effective than saline lavage [23]. Finally, a rising albumin concentration in wound fluids during operations decreases the antibacterial activity of polihexanide antiseptics [24]. Consequently, the early application of a rinse solution onto the subcutaneous tissue could be advantageous.

The aim of this trial was to investigate if the early application of polihexanide to the surgical wound, which would result in a longer application time for the antiseptic, could be advantageous in the prevention of SSI compared with a short application time at the end of the procedure. As control the late application of polihexanide was chosen, as there are many good indications for its efficacy and it is standardized in our department. The findings of this pilot trial will create the basis for a formal sample size calculation.

2. Material and methods

2.1. Participants

This study was performed by the department of abdominal surgery of a district teaching hospital. Between August 2014 and March 2015, all patients who were admitted to our department and consented to abdominal surgery were screened for study eligibility by the primary investigators. All adults scheduled for an elective laparotomy, including gastrointestinal, colorectal, hepatobiliary or pancreatic surgery, were included if informed consent was obtained preoperatively. Study exclusion criteria included a known previous allergic reaction to polihexanide or a refusal to participate. All patients were asked to visit the outpatient clinic for a follow-up examination on day 30 postoperatively. The demographics (age, gender and body mass index), diagnosis, nutritional status (serum level of albumin), anaemia (level of haemoglobin), use of steroid-containing drugs, comorbidities (cardiovascular disease, pulmonary disease or diabetes) and the American Society of Anesthesiologists (ASA) score were recorded for each patient.

For a control group, we included 57 consecutive patients who were operated on at our department for the same elective indications between March and July 2014. These patients were analysed retrospectively using electronic medical records and patient databases. Background data and the primary and secondary end points were collected in the same manner.

2.2. Surgical technique

A standard antibiotic prophylaxis (ampicillin 2 g iv/sulbactam 1 g iv) was administered preoperatively. Patients with conditions traditionally associated with infections (*e.g.* cholangitis, diverticulitis) received a different selection of antibiotic therapy (ceftriaxone 2 g iv/metronidazole 500 mg iv or meropenem 1 g iv). In these cases, postoperative therapy was given at the surgeon's discretion. In cases of suspected allergies, the surgeon could administer an alternative regimen (such as levofloxacin 500 mg iv/metronidazole 500 mg iv). A safety check-list was used perioperatively.

Preoperative skin preparation was performed with at least three swabs soaked with disinfectant applied in a standardized manner to wash the abdominal skin (Softasept®N, B.Braun AG, Melsungen, Germany). All operations were performed according to a standardized technique, and were performed or supervised (five cases) by six certified abdominal surgeons. The skin was incised by a scalpel and the dissection of the subcutaneous tissue and aponeurosis was made with a monopolar cutting electrode. The incision was made transversally for pancreatic or hepatobiliary surgery. A midline incision was used for the remaining procedures. The abdomen was closed with triclosan-coated polydioxanone sutures (PDS II PLUS®; Ethicon, Johnson & Johnson, New Brunswick, NJ, USA) using a continuous suture technique. No subcutaneous drains or sutures were used and skin closure was accomplished using surgical skin staples. A closed-system for intraabdominal drainage was routinely used, inserted through a separate incision remote from the main incision site (Blake™ Silicone Drain, Ethicon, Somerville, NJ, USA).

The use of polihexanide consisted of irrigating the subcutaneous tissue with Lavanid®2 (SERAG-WIESSNER GmbH&Co. KG, Naila, Germany), which contains 0.04% polihexanide. In the intervention group ("long") the subcutaneous tissue was irrigated prior to the initial incision through the aponeurosis. During the operation, the incision site was protected with abdominal swabs soaked in polihexanide. After closing the fascia, the subcutaneous tissue was irrigated again with polihexanide prior to the final closure of the skin. At least 250 mL of irrigation had to be used.

The subcutaneous tissue of the control group ("short") was not irrigated after the initial incision. The incision site was protected with saline-soaked abdominal swabs. After fascial closure, irrigation with polihexanide followed, and the active substance was removed by rinsing the tissue with saline solution prior to skin closure.

Perioperative treatment followed fast-track recommendations [25]. Nasogastric tubes were removed by the first postoperative day (POD1) at the latest. Clear drinks were provided on the first evening postoperatively. If tolerated, liquid food was allowed on the first postoperative day (POD1), and solid food on POD2. Dressings were removed on POD2, and showering was then allowed. Mobilization started from POD1.

2.3. Ethical considerations, motivation and funding

The protocol for this trial conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in its approval by the ethics committee of the Medical Association of Baden-Württemberg, Germany. Informed consent was obtained from each patient. The study was registered at the German Clinical Trials Register (DRKS00006004).

The trial was an investigator-initiated trial. We conducted the trial with our own resources.