

June 16, 2020  
Keio University School of Medicine

## **Olanexidine, a New Antiseptic Produced Domestically in Japan, Shown to Halve the Occurrence of Surgical Site Infections in Randomized Controlled Trial**

A research team at the Keio University School of Medicine has demonstrated that olanexidine, a new antiseptic produced domestically in Japan, can significantly reduce the occurrence of surgical site infection (SSI) and superficial incisional SSI. Olanexidine was proven to outperform aqueous povidone-iodine, an antiseptic that is currently in wide use at clean-contaminated surgical sites in Japan. The team was led by Associate Professor Hideaki Obara, Assistant Professor Masashi Takeuchi, and Professor Yuko Kitagawa of the Department of Surgery.

Surgical site infections (SSI) are one of the most common types of post-surgical infection. SSI can cause post-operative death and can lead to patient distress, including prolonged hospitalization and impaired cosmetic outcomes as well as an increase in health-care costs. SSI is reported to occur in ten to thirty percent of all gastrointestinal and hepatobiliary pancreatic surgeries.

The most basic and important measure to reduce the risk of SSI is to perform skin antisepsis with an antiseptic at the incision site immediately ahead of surgery. For more than half a century, doctors in Japan have mainly used iodine-based disinfectants for skin antisepsis. Still, in recent years, there has been an increase in reports of SSI caused by antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE). This means that there is a real need for the development of new disinfectants that can protect against antibiotic-resistant bacteria such as these.

This new antiseptic, Olanedine® Antiseptic Solution 1.5% OR, was developed by Otsuka Pharmaceutical Factory in Tokushima, Japan, and has been commercially available in Japan since 2015. Its main ingredient is olanexidine gluconate, which has a significant effect on preventing the growth of antibiotic-resistant bacterias like those mentioned above.

This clinical trial was conducted between June 10, 2018, and April 18, 2019. Of the 883 patients that were assessed, 587 patients were deemed to be eligible, and ahead of surgery, 294 received olanexidine, with the other 293 receiving aqueous povidone-iodine. Within thirty days following surgery, SSI occurred in 19 (6.5%) of the olanexidine group patients, less than half of the 39 cases (13.3%) that occurred in the povidone-iodine group.

The findings can be applied not only to the field of gastroenterological surgery but also to surgery and treatment in other fields of medicine and are expected to contribute to SSI management for a wide range of surgical patients by providing new SSI prevention procedures and could potentially lead to reduced medical costs.

The results of this research were published in the electronic version of the British international medical journal, *The Lancet Infectious Diseases*, on June 15 (BST).

## **1. Research Background**

Surgical site infections (SSI) are one of the most common types of post-surgical infections in a number of surgical specialties, including gastrointestinal, orthopedic, and obstetric and gynecologic surgery. It is also not uncommon for SSI to cause post-operative death. SSI can lead to prolonged hospitalization, impaired cosmetic outcomes, and an increase in health-care costs. In the United States, medical care costs due to SSI were estimated to be ten billion dollars annually, and in Japan, the cost of treating SSI is said to be more than 300,000 yen per patient. In Japan, it has been reported that among gastrointestinal surgeries to treat conditions such as gastric, colon, and liver cancer, one in every ten patients develops an SSI. The prevention of SSI is a very important issue not only for patients, but for all medical staff involved in the surgery, which has led to many different attempts at preventive measures. Skin antisepsis of the surgical site is the most basic and important measure against SSI and is often done using alcohol- and iodine-based disinfectants. However, there have been strong warnings against alcohol-based disinfectants due to the risk of fire when using an electric scalpel (PMDA Medical Safety Information No. 15 2010), and in Japan, iodine-based disinfectants have been the main method of skin antisepsis for more than half a century. In recent years, however, there has been an increase in reports of SSI caused by antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE), and there is a real need for the development of new disinfectants that can protect against antibiotic-resistant bacteria such as these.

Olanexidine antiseptic, a new type of domestically produced disinfectant, was launched in 2015 by Otsuka Pharmaceutical Factory, Inc. This disinfectant is a novel biguanide antiseptic whose active ingredient is olanexidine gluconate, and pharmacological and animal studies have confirmed that it has a significant and fast-acting effect on preventing the growth of not just general bacteria, but antibiotic-resistant bacteria such as MRSA, VRE, *Pseudomonas aeruginosa*, and even *Serratia marcescens* and *Burkholderia cepacia*. However, since there had been no scientific comparative studies of conventional disinfectants, and the manufacturer, Otsuka Pharmaceutical Factory, had no plans for an industry-sponsored trial, our research team independently organized and conducted its own investigator-initiated, randomized controlled trial.

This study was conducted jointly by Keio University and four affiliate institutions with patients over the age of 20 who were scheduled for class II (clean-contaminated) gastrointestinal (esophagus, stomach, duodenum, small intestine, large intestine, liver, biliary tract, pancreas) surgery under general anesthesia. Patients were randomly divided into two groups, and immediately before surgery, one group used olanexidine gluconate as a surgical site disinfectant, while the other used 10% aqueous povidone-iodine, which is an iodine disinfectant. 597 patients were enrolled in the study between June 2018 and April 2019. Our primary endpoint was the occurrence of SSI within thirty days following surgery. As secondary endpoints, we evaluated the side effect rate of superficial incisional SSI, deep incisional SSI, and organ/space SSI within 30 days after surgery as well as the positive wound culture rate and the resulting bacterial strains.

## **2. Research Significance and Future Development**

Of the 597 patients that were registered, 587 patients were analyzed, with one group of 294 receiving olanexidine, and the other group of 293 receiving aqueous povidone-iodine. Our primary endpoint was the number of SSIs occurring within thirty days following surgery. SSI occurred in 13.3% (39 cases) of the povidone-iodine group patients but was halved to only 6.5% (9 cases) in the olanexidine group. The SSI rate for surface incision also decreased by using olanexidine, from 4.4% (13 cases) in the povidone-iodine group to 1.3% (4 cases) in the olanexidine group. In addition, olanexidine did not raise any new safety concerns.

This study revealed that olanexidine, a new surgical site antiseptic, significantly reduces surgical site infection compared to widely used iodine-based antiseptics. The study also provides strong evidence for the rest of the world regarding this new, domestically produced surgical site antiseptic. Surgical site disinfection is the most basic and easily performed preventive measure against surgical site infection (SSI), and the results of this study

are considered to be useful not only for gastrointestinal surgery but also in surgery in a wide range of fields that include obstetric, gynecologic, and orthopedic surgery. Olanexidine antiseptics are currently sold only within Japan, but it is expected that the results of this study could lead to preparation for international sales in the near future.

### **3. Notes**

This research was supported by the 2017 Ohyama Health Foundation Academic Research Grant.

### **4. Research Paper**

Title : Aqueous olanexidine versus aqueous povidone-iodine for surgical skin antisepsis on the incidence of surgical site infections after clean-contaminated surgery: a multicentre, prospective, blinded-endpoint, randomised controlled trial

Japanese Title : 手術部位感染に対するオラネキシジングルコン酸塩消毒薬 vs 水溶性ポビドンヨード消毒薬の多施設共同、前向き、盲検エンドポイント、無作為化比較試験

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Publication : The Lancet Infectious Diseases

DOI : 10.1016/S1473-3099(20)30225-5

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