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Faculty of Medicine

ANTIBACTERIAL IODINE-SUPPORTED TITANIUM IMPLANTS

An Essay

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Ag-i-: Silver iodide

BC: Before Christ.

CRP: C-reactive protein

DNA: Deoxyribonucleic acid

E.coli: Escherichia coli.

EDTA: Ethylenediaminetetraacetic acid

MRSA: Methicillin-resistant Staphylococcus aureus

NO: Nitric oxide

ONOO−: Peroxynitrite

PBS: Phosphate-buffered saline.

PMMA: Polymethylmethacrylate

PVP-I: Povidone-iodine.

Ti-I: Iodine- supported titanium

WBC: White blood cell

Introduction

Infection continues to plague all medical disciplines that relay on implantation of a foreign object. In orthopedics, while a diversity of organisms is present in deep infection, the dominant bacteria are Gram-positive pathogens, with Staphylococcus aureus and the coagulase-negative staphylococci especially prevalent. [1]

In cases of devastating trauma despite aggressive antibiotic prophylaxis and delay of hardware placement, infection occurs frequently. Pathogen colonization of hardware is enhanced by the host response to implantation. Specifically, the host rapidly coats implanted materials with serum proteins that promote cell recruitment and tissue repair. Un fortunately, these same serum proteins are used by pathogens for adhesion and virulence. [2]

The problem is further compounded by activation of an inflammatory response as well as the complement system upon presentation of these adsorbed proteins. These events, including attenuated activation of phagocytic cells, blunt the local immune response creating an opportunity for pathogen colonization. [3]

When prophylaxis does not prevent infection, the treatment of implant-related infection becomes a challenge for the surgeon. Treatment is usually a combination of surgery, based on surgical debridement including the removal of necrotic tissue, bone

sequesters and often the implant itself, and local and systemic antibiotic therapy. In addition to surgical issues, a microbiological problem has to be considered. Bacteria adhering to the surface of implants change their biological behavior. They produce a biofilm that creates a microenvironment protective against many antimicrobial agents. Moreover, they reduce their metabolic activity and thus increase their generation times. [4]

Because antibiotics act on growing bacteria, the minimum inhibitory concentrations (MIC) are increased with bacteria that have reduced metabolic activity. As systemic antibiotics cannot reach such a high concentration at the local site, they become ineffective. To solve this problem, local antibiotics can be used to achieve much higher concentration (up to 1000 fold) than systemic antibiotics can achieve.

On the other hand, the risk of systemic toxicity and side effects of parenteral antibiotics can be reduced. Owing to a higher drug concentration in the relevant tissues, effectiveness is enhanced, which reduces the duration of treatment. To promote the surface compatibility of orthopedic implants, and to generate osteoinductive materials (which stimulate osteogenesis or formation of new bone), surface modifications can be used.

To date, different surface modification strategies for orthopedic implants have been investigated, including:

(a) Addition of materials of desired functions to the surface e.g. bioactive ceramic coatings.

(b) Conversion of the existing surface into more desirable chemistries and/or topographies.

(c) Removal of material from the existing surface to create new relevant topographies. [5]

In the treatment of infections, elemental iodine is of significance as a prospective anti-infective agent. Iodine has intrinsic chemical properties which could be exploited in conferring to implant devices novel and efficacious anti-infective activities in the treatment and prevention of opportunistic infections. Iodine has been used for over 150 years in various formulations as a sterilizing agent.

In this study, titanium implants were used with surfaces that were modified using anodization. Biocompatible metal-oxide implants have current clinical applications in orthopedic and dental implants. The excellent biocompatibility of titanium is reportedly attributable to the stable oxide that readily forms on its metal surfaces. The composition of highly adhesive anodic oxide films that form through anodization is dependent on the

electrolyte composition. Povodine iodine can also be used as an electrolyte, resulting in the formation of an adhesive, porous anodic oxide with the antiseptic properties of iodine. [6]

Aim of the Study

The aim of this essay is evaluating the antibacterial activity of iodine- supported titanium (Ti-I) and its impact on post-implant infection, as well as determining the potential suitability of (Ti-I) as a biomaterial.

Iodine As Anti Infective Agent

For more than 150 years, iodine has been used for the prevention of infection and for the treatment of wounds.

Use of its beneficial impact had even existed much earlier without any actual awareness of the active substance. Already in the Greek Age (4th century BC), Theophrastus, Aristotle's pupil and first expert in medical plants, described the use of seaweeds and other plants in refreshing and relieving pain after sun burn wounds.

During Napoleon's Egyptian campaign (1798-1801), wounded soldiers were treated with extracts from seaweeds and other plants enriched with iodine at high concentrations from sea water. [7] Also during the American Civil War (1863), the use of iodine for disinfections was widespread.

Even if iodine-containing plants were well used before, the natural element iodine was only discovered in 1811 by the Dijon chemist Bernard Courtois. It was given its name from the Greek ioeides meaning "violet coloured", because of the intensely violet colour of its vapours. [7] Iodine's bactericidal efficacy was first described scientifically by Davaine [8] in 1880 and it was only between the 19th and 20th century that surgeons started to use iodine as a preoperative disinfectant.

At that time, iodine was widely used as a particular iodine compound, called iodoform (triiodomethane, CHI3) and as ethylic iodine tincture with all the disadvantages of lacking stability and highly aggressive action on skin and mucosa. [8]

Already in 1919 Alexander Fleming stated that, in considering and estimating the value of an antiseptic it was probably more important to study the effect on tissues than on bacteria. [9]

It was the development of the iodophors (substances that can carry Iodium, e.g. povidone-iodine), and the detoxification of iodine by binding it to macromolecules by Schelanski which made the large-scale use of this highly effective microbiocidal possible. [10]

Elemental iodine is a violet-black non-metallic crystalline solid, with an atomic weight of 126.904, which readily sublimes to form a pungent irritating violet vapour. Its solubility in water is only 1:3000.

Iodine is an essential nutrient required for synthesis of thyroid hormones and the body requires 100-200μg iodine per day. Iodine compounds have diverse uses: potassium iodate and sodium iodide are used to treat iodine deficiency diseases, other iodine salts are used in expectorants and as diuretics. [11], [12]

As a general rule, less is known about the mode of action of antiseptic agents compared to antibiotics. Antiseptic agents