A 40 years old lady presented with right iliac fossa pain of 10 days duration. The patient gave a history of accidentally ingesting a metal object (drilling bit) during a dental procedure prior to pain. There was few episodes of vomiting. She has a previous history of laparoscopic sleeve gastrectomy, bilateral tubal ligation and abdominoplasty. Her abdomen was tender in the right iliac fossa with guarding and positive rebound tenderness. The Laboratory investigation were within accepted range. The patient had an Abdominal X-ray that showed a long pointed metal object in the right lower quadrant (figure 1).

Computerised tomography (CT) of the abdomen showed a metallic foreign body at the right pelvic region with slight motion between the pre and post contrast scans. No free or localised collection seen. No pneumoperitonium.

The patient underwent a diagnostic laparoscopy, the whole abdomen was inspected with no fluid or bleeding in the abdomen. An inflamed appendix was seen and a metal pointed object was perforating the appendix. An appendectomy was performed. Ovaries were normal and no abnormality detected in small bowel (figure 2).

Histopathology showed an acute necrotising appendicitis with periappendicitis.

Foreign body ingestions are common among children and mentally disabled. The majority of the ingested material pass through the alimentary tract spontaneously (80%). Impaction, perforation or obstruction occurs <1% and require surgery; these occur at gastrointestinal acute angulations e.g.: duodenojejunal junction, iliocecal valve, appendix, narrowing e.g: stricture or adhesions or previous GI surgery or anomaly (1). Most of the ingested objects are coins, magnets and button batteries. The guideline management of ingested material depends on the timing of ingestion, type, size, shape and location of the object.

Appendicitis caused by foreign body ingestion is very rare and few case reports documented it. these studies concluded that mostly long sharp objects would lodge in GI angulations and can be symptomatic with in days to weeks; however, round blunted objects usually remain dormant for months or even years till it become symptomatic. Also complications e.g: abscess formation or fistula can occur.

Conclusion, appendicitis induced by foreign body is rare and present either early or late according to the shape of the object.

References:
INTRODUCTION

Increasing resistance of bacteria to antibiotics creates a demand for development of alternative methods of treatment. Photodynamic inactivation (PDI) of microbes, which is based on the combination of a non-toxic light-absorbing compound, called photosensitizer (PS) and illumination with visible light, has shown promising results for treatment of localized infections caused by Gram-positive and Gram-negative bacteria. Its further development as an alternative of antibiotics depends on availability of photosensitizer (PS) and illumination with visible light, has shown promising results for treatment of localized infections caused by effective and selective PSs that do not provoke resistance against the photodynamic treatment or against antibiotics. The aim of this study was to investigate how bacteria respond to prolonged exposure to sublethal PDI with a porphyrin-based PS and how efficient is PDI against antibiotic-resistant Gram-negative and Gram-positive strains.

RESULTS

The purpose of the initial experiments was to select a sublethal dose of PDI which would be subsequently used in experiments testing development of resistance. Fig. 2 shows that at 1.0 μM ZnTnHex-2-PyP inhibits MTT reduction by ~80% and kills ~99% of the cells. Based on these results, ZnTnHex-2-PyP was applied at 1.0 μM for performing ten consecutive cycles of PDI and regrowth of survivors.

Fig. 2 Relationship between ZnTnHex-2-PyP concentration and E. coli inactivation. Stationary phase E. coli culture was incubated 30 min with PS and illuminated for 20 min at a fluence of 37 mW/cm². Cell viability was determined by the MTT assay (A) and by plating and enumeration of colonies (B). Mean ± SD of two separate experiments, each sample run in triplicate, is presented.

Results displayed in Fig. 3 and Fig. 4 demonstrate that after ten cycles of sublethal photodynamic treatment and regrowth, survivors were as sensitive to PDI as were the non-treated cells. During the ten cycles of treatment, E. coli could not develop protection against PDI-induced suppression of metabolism (Fig. 3) or loss of viability (Fig. 4).

Fig. 3. Effect of sublethal photodynamic treatment and regrowth on suppression of cell metabolism by PDI.

Fig. 4. Effect of repeated sublethal photodynamic treatment on E. coli survival after PDI treatment.

EXPERIMENTAL PROCEDURE

The tetra-cationic Zn(II) meso-tetraakis(N-hexylpyridinium -2-yl)porphyrin (ZnP, ZnTnHex-2-PyP), shown in Fig. 1, was used as a photosensitizer. The compound was chosen because of its high antimicrobial photoefficiency.

E. coli and S. aureus resistant to multiple antibiotics, and corresponding antibiotic-sensitive strains, were exposed to sublethal PS concentrations and light intensity. Effect on cell metabolic activity was determined by the MTT [3-[4,5-dimethylthiazol-2-y]-2,5-diphenyltetrazolium bromide] assay, and ability to proliferate was assessed by the clonogenic assay. All experiments were repeated at least two times with 3 - 5 replicates. Statistical analysis was performed using SigmaPlot 11.0.

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Conclusions:

It has been reported that prolonged exposure of S. aureus to a Zn (II) phthalocyanine derivative caused increased resistance against the dark toxicity of the PS, eventually due to activation of efflux pumps or structural changes in the plasma membrane, which limit its uptake. It might be expected that repeated sublethal PDI exposure of E. coli can induce mechanisms preventing the uptake of the ZnP, and as a consequence, decreasing its photo-efficiency. To test PDI effects on dark toxicity, after ten cycles of PDI treatment and regrowth, E. coli was incubated in the dark with ZnTnHex-2-PyP at a concentration range of 2 – 20 μM. Fig. 5 shows that about 20% suppression of MTT reduction was caused by 10 μM ZnP, and that at 20 μM the PS suppressed E. coli metabolic activity by about 70%. No difference between the non-treated and the sublethal PDI-treated cells was observed with respect to the dark toxicity of ZnTnHex-2-PyP.

A more accurate approach in investigating development of resistance would be sublethal PDI exposure allowing bacterial cultures to grow continuously. Our preliminary investigations demonstrated that E. coli cultures incubated in LB medium containing up to 2.0 μM of ZnTnHex-2-PyP did not grow if exposed to light with fluence of 1.0 mW/cm², but did grow when light intensity was decreased to half of that value. Therefore, to allow cultures to grow under PDI conditions, overnight E. coli cultures were diluted 100 fold in LB medium containing 0.5, 1.0 or 2.0 μM ZnTnHex-2-PyP and allowed to grow aerobically for 48 h under constant illumination of 0.5 mW/cm². Results show (Fig. 6) that continuous growth under PDI conditions did not provoke resistance against PDI. To confirm that growth under sublethal PDI conditions does not select resistant mutants, PDI-treated aliquots were diluted again 100 fold in LB medium and re-exposed for 48 hours to the same treatment. After three 48 hour cycles of sublethal PDI exposure, sensitivity to PDI treatment was tested again. Results were not different than those displayed in Fig. 6.

Resistance to a single antibiotic is frequently accompanied by increased resistance to other antimicrobial agents. It might be expected that antibiotic-resistant bacteria would be less sensitive to PDI treatment with ZnTnHex-2-PyP than their antibiotic-sensitive counterparts. To test such a possibility, PDI sensitivity of antibiotic-resistant clinical isolates and antibiotic-sensitive strains was compared. Fig. 7 shows that photodynamic treatment with ZnTnHex-2-PyP suppresses MTT reduction to the same extent in antibiotic-sensitive and antibiotic-resistant E. coli and S. aureus. Similar results were obtained when cell viability was determined by plating and counting colonies (Fig. 8).

Fig. 7. Inactivation of antibiotic sensitive and antibiotic-resistant E. coli and S. aureus by PDI. Blue bars, cells illuminated in the absence of a PS, red bars, cells illuminated in the presence of ZnTnHex-2-PyP.

Fig. 8. Photodynamic killing of antibiotic-resistant E. coli (A) and S. aureus (B). Experimental conditions were as in Fig. 2.
Lutein modulates transcription dysregulation of adhesion molecules and spermatogenesis transcription factors induced by testicular ischemia reperfusion injury: It could SAFE

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Introduction
Ischemia reperfusion injury (IRI) is implicated in the development of testicular damage following torsion and detorsion. Testicular IRI (tIRI) triggers a complex cascade of cellular and molecular reactions that involves the generation of reactive oxygen species and induces testicular oxidative stress and germ cell apoptosis. A devastating outcome of tIRI is the damage to spermatogenesis and possible increased risk of infertility. Preventing spermatogenesis is enabled by the highly coordinated restructuring of the blood-testis barrier (BTB) found between adjacent Sertoli cells. Although the mechanism of junction assembly and disassembly at the BTB remains unclear, any dysregulation of the BTB and Sertoli cell junctions can result in male infertility. Regulation of spermatogenesis is also governed by local cell-cell interactions within Sertoli cells and between Sertoli cells and germ cells. Such interactions are mediated via cellular junction proteins and their adaptors, which form specialized adhesion junctions, tight junctions, gap junctions, cell polarity proteins, and proteins regulating paracellular diffusion. In addition, spermatogenesis is subjected to a cascade of gene expression regulation, whereby specific master transcription factors (TFs) are responsible for switching on and off the different stages of spermatogenesis.

Objectives
The present study seeks to examine whether the mRNA expression of spermatogenesis master gene switches and some of the major adhesion molecules of the BTB is deregulated during tIRI. The effects of lutein, a powerful antioxidant, is also studied to show its effect on tIRI-induced oxidative stress and whether it can prevent damage to spermatogenesis and gene expression modulation. The involvement of the survivor activating factor enhancement (SAFE) pathway is also investigated.

Materials and Methods
Three groups of male Sprague-Dawley rats (6 rats/group) were used: sham, unilateral tIRI (1 hr ischemia followed by 4 hrs reperfusion), and tIRI + lutein (0.2 mg/kg, i.p.). Testicular tissue was evaluated for the gene expression of spermatogenesis master TFs and adhesion molecules by real-time PCR. Damage to spermatogenesis was evaluated by Johnson scoring, while activation of caspase 8 pathway and oxidative stress markers was assessed by immunohistochemical assays. The effect of tIRI and lutein treatment on the SAFE pathway was determined using ELISA.

Conclusions
1- Testicular IRI was associated with dysregulation of the transcription levels of spermatogenesis TFs and AMs, which could have contributed to the histological changes observed in the seminiferous tubules.
2- The structural properties of lutein that make it a strong antioxidant prevented tIRI-induced oxidative stress, germ cell apoptosis, and modulation of mRNA expression of spermatogenesis-related genes.
3- Lutein could have potential therapeutic value against tIRI, however, its reactive potency still needs to be compared with that of other antioxidants with similar effects to identify the compound with the best therapeutic value for testicular torsion-detorsion patients in clinical settings.

Fig. 1 H&E and TUNEL staining of ipsilateral testicular tissue. A&D. Sham testis showing normal histological morphology and low germ cell apoptosis (GCA). B&E. The tIRI-subjected testes displayed degenerative changes including testicular atrophy, reduction in tubular size and enlarged interstitium with increased GCA. C & F. Lutein treatment reversed all histological changes to sham and reduced GCA.

Fig. 2 Increased levels of (A) total antioxidant capacity (TAC) and (B) malondialdehyde (MDA) concentration were measured in tIRI-subjected testes compared to sham (P < 0.0001 and P < 0.0001, respectively). In parallel, increased levels of caspase 8 and caspase 3 were measured after tIRI compared to sham (P < 0.0001 and P < 0.0001, respectively). Lutein treatment (0.2 mg/kg) normalized the levels of TAC, MDA, and caspases 8 and 3. The data are expressed as mean ± SEM.

Fig. 3 Transcriptional regulation of (A) spermatogenesis transcription factors (CREM, TEF2 and RFX2) and (B) adhesion molecules (N-cadherin,nectin 2, occluding, claudin-31, and connexin-43). RT and real-time PCR was used to calculate the fold change in the mRNA expression, which were significantly reduced during tIRI but normalized upon lutein treatment (*P < 0.05 compared to sham, **P < 0.05 compared to tIRI). Data are expressed as mean ± SEM (n = 6). * and ** P < 0.05, significantly different from sham and tIRI groups, respectively.

Fig. 4 Effect of tIRI and lutein treatment (0.2 mg/kg) on SAFE signaling molecules. Graphs represent quantitative differences in the expression of (A) TNFa (P < 0.0001 tIRI vs. sham and *P < 0.0001 lutein treatment vs. tIRI), (B) TNFR1 (P = 0.0042 tIRI vs. sham and *P = lutein treatment vs. tIRI), (C) pan and phosphorylated forms of JAK (P < 0.0001 tIRI vs. sham and *P < 0.0001 lutein treatment vs. tIRI), (D) STAT3 (*P = 0.036 tIRI vs. sham, and *P = 0.0007 lutein treatment vs. tIRI). Levels of testicular TNF-α and TNFR1 were measured by ELISA, while phosphorylation of JAK and STAT3 were measured by phosphorylation ELISA assays. Data are expressed as mean ± SEM (n = 6).