

Granulated sugar for adjuvant treatment of surgical wound infection due to multi-drug-resistant pathogens in a child with sarcoma: a case report and literature review

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SUMMARY

The use of sugar for treating wounds which are difficult to heal and positive to resistant pathogens has already been documented. The authors describe the successful treatment by direct instillation of granular sugar in the antibiotic-resistant infected surgical site wound of a child with sarcoma. Sugar instillation in the extended spectrum beta-lactamase (ESBL)-producing *Enterobacter cloacae* positive wound, in addition to systemic

treatment with meropenem and levofloxacin, allowed culture negativization in six days and complete wound healing in 30 days. These results make the use of sugar an attractive option for wounds which are difficult to treat, even in an immunocompromised child.

Keywords: wound infection, sugar, antibiotic resistance, paediatrics

INTRODUCTION

Surgical wound infections may represent important and difficult to treat complications in cancer patients because of the concomitant presence of surgical trauma, inflammation, poor antibiotic penetration in skin and soft tissue, and impaired local and systemic defenses due to immunosuppression [1].

The situation can be even worst in presence of infections due to resistant pathogens, when drugs

with poor or unknown skin and soft tissue (SST) penetration could be needed, with the risk of inefficacy and possibly resistance selection [2-5].

In the past such infections were treated locally with packed gauze soaked in antiseptic solution, *e.g.* eusol, chlorhexidine or iodine based solutions, together with systemic antibiotics [6]. Noteworthy, *in vitro* and clinical data suggest that also honey and sugar paste can be effective in clearing wound infection and improving healing [7-9].

We describe a case of surgical wound infection due to antibiotic resistant Gram-negative treated with direct instillation of granular sugar and systemic antibiotics in a child receiving antineoplastic chemotherapy.

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■ CASE REPORT

An 8-year-old boy affected with schwannoma of the right flank and iliac crest bone was transferred in our center for treatment of surgical wound infection. At time of first observation the patient was febrile ($>38^{\circ}\text{C}$) and the surgical wound was painful and with purulent discharge. Antibiotic therapy with piperacillin-tazobactam (100 mg/kg/dose of piperacillin q8h in 3 hours infusions) and vancomycin (10 mg/kg q6h in 1 hour infusions) was started with rapid general improvement. Wound cultures yielded a strain of *Enterobacter cloacae* susceptible to piperacillin-tazobactam (MIC $<4/4$ mg/L) and therefore, vancomycin was withdrawn. However, the wound was still painful, discharging pus, and without granulation tissue and still positive for the same pathogen after more than 1 week of this therapy. At this time the strain of *E. cloacae* still isolated from the secreting wound resulted resistant to piperacillin-tazobactam (MIC $>64/4$ mg/L) by production of extended spectrum beta-lactamase (ESBL). Therefore meropenem (20 mg/kg q8 h in 2 hours infusions) was administered in combination with levofloxacin (10 mg/kg q12 h), both drugs active against the isolated strain. One week later, the wound appeared still dehiscent, necrotic, macerated with a score 21, according to Knighton, et al. (Figure 1a), and cultures were still positive for the same pathogen [7, 10-14]. After obtaining parental consent, we proceeded to surgical removal of the necrotic tissue and associated antibiotics with local disposition of 5 g of commercial granulated sugar pre-packaged in sachets, further covered with sterile dressing of the infected wound.

Dressings and sugar disposition were changed twice daily for the first few days to facilitate quick debridement, progressing to daily dressings when the exudate level diminished. After 5 days of this treatment the patient reported a reduction in wound pain. In the following days pus drainage stopped and the wound progressively improved (score 11) (Figure 1b) [7, 11-14].

Subsequent cultures were all negative. On day 30 no evidence of infection was present and sugar dressing and antibiotics stopped. No adverse event was observed during treatment period.

■ DISCUSSION

We report a case of difficult-to-treat surgical wound infection by an ESBL-producing *Enterobacter* in a cancer child, that healed with the addition of topical, commercial granulated sugar combined with antibiotics after failure of other strategies based only on antibiotic administration [3, 4, 14]. A possible explanation of this phenomenon was the presence of low, ineffective antibiotic tissue concentration in a complicated SST infection. This aspect could become even worst if drugs with scarce skin and soft tissue concentrations must be administered.

The efficacy of topical disaccharides (in the form of either sugar or honey) to cleanse infected wounds and facilitate healing has been recognized from many centuries back to ancient Egypt and Medieval Europe [7, 15]. Sugar granules and honey have osmotic action that is thermodynamically related to water activity, pH and osmotic effects, and compete with bacteria and fungi for the water,

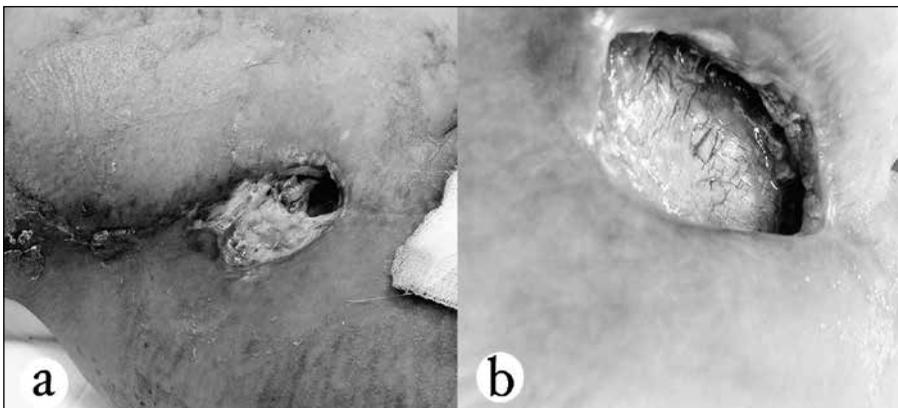


Figure 1 - Surgical wound infection with ESBL-producing *E. cloacae* a) after 1 week of administration of prolonged infusion meropenem and levofloxacin; b) 1 weeks after association of granular sugar to antibiotics.

determining water deprivation and disruptions of bacterial and fungal cell membranes [7, 11-14]. Their effect is also mediated by the production of hydrogen peroxide, which is released in an exuding wound at a controlled rate at a level that is not toxic to host tissue [8-23]. Moreover honey also possesses anti-inflammatory activity and stimulate immune responses, via an increased release of tumor necrosis factor-alpha, interleukin-1beta and interleukin-6 [9]. A comprehensive MEDLINE search using as keywords "infected wounds and sugar or honey", without temporal limits, showed that sugar/honey therapy has been used in many SST infection, including surgical wound infections in the past, and is still used as a wound dressing in the tropics, often applied in its granulated form or as a paste [11, 16, 22-24]. All these considerations lead us to the choice of an unconventional therapy that finally resulted effective. Since sugar is not metabolized outside the intestinal tract, its local application could not be expected to lead to systemic absorption. However, adverse events have been reported in association with local application of sugar/honey including significant irritation of local tissues, hyperglycemia, electrolyte imbalance and one case of acute renal failure and severe hyponatremia in presence of large open wounds [22]. None of these occurred in our patient.

In this case we used sugar sachets packed according to European Union directive 2001/111/CE for sugar intended for human consumption. These compounds are not for medical uses and therefore we required parental consent. Subsequently a clinical protocol for its use in extreme conditions was submitted to the Internal Review Board.

We recognize that the available data have limited quality, as reporting poor quality, poor validity or poor sample size studies and therefore more studies are needed to confirm our observation. Randomized clinical trials should be the golden standard for analyzing the effectiveness of this procedure, but the low number of patients presenting at present with this type of complication could impair the reliability of a trial that necessarily will require a large number of patients to be enrolled, with a very long accrual period, and the results waited (or diluted) during a very long period of time, possibly reducing their reliability. This could be not compatible with clinical needs. Therefore, we believe that the present case report,

suggesting that topical granular sugar dressing could represent an effective complementary treatment of surgical wound infections due to antibiotic resistant pathogens, could be useful for the everyday clinical practice, especially in a time when the availability of new antibiotics active against resistant bacteria and with favorable pharmacokinetics is lacking.

Conflicts of interest

None

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