

Bee honey added to the surgical management of intra-abdominal sepsis. Report of two cases

Miel de abeja sumada al manejo quirúrgico de la sepsis intraabdominal. Informe de dos casos

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ABSTRACT

Among the attributes of bee honey, its antimicrobial properties stand out. In foreign countries, there are already therapeutic kinds of honey, especially for the treatment of wounds. There is ongoing research with experimental studies that have used honey even for the prevention of intra-abdominal adhesions due to peritonitis. Surgical treatment of intra-abdominal sepsis (IAS) may include peritoneal lavage and other strategies according to its severity. We report two severe cases of this condition with an unfavorable prognosis, in which intra-abdominal honey was used as an adjunct, expecting an antimicrobial activity. Clinical progress in both patients was favorable. The use of honey is supported by literature and previous experience, and by attempts to prevent persistent peritonitis. From what is known about honey, benefits in IAS may be expected, since its use looks promising. Although recognizing its limitations, honey could be an adjuvant to therapeutic interventions or surgical approaches when necessary.

RESUMEN

Entre los atributos encontrados en la miel de abeja destaca su capacidad antimicrobiana; en el extranjero existen ya mieles terapéuticas, sobre todo para el tratamiento de las heridas. La investigación continúa con estudios experimentales que han ocupado la miel incluso en la prevención de adherencias intraabdominales por peritonitis. El tratamiento quirúrgico de la sepsis intraabdominal (SIA) puede incluir lavado peritoneal y estrategias de acuerdo a la gravedad. Se exponen dos casos clínicos con esta patología —graves y con mal pronóstico— en donde se sumó la aplicación de miel dentro de la cavidad abdominal, en busca de su acción antimicrobiana. La evolución fue favorable en ambos pacientes y sustenta lo hallado en la literatura, la experiencia previa y su uso para tratar de evitar peritonitis persistente. Por todo lo conocido de la miel de abeja, es de esperarse que sea benéfica en la SIA, por lo que es prometedora su utilidad. Sin dejar de reconocer las limitaciones en su uso, podría agregarse a las acciones del tratamiento y/o estrategias quirúrgicas cuando sea necesario.

INTRODUCTION

Honey is a natural product made up from the nectar of flowers in the upper digestive tract of honeybees. Its composition will depend on the origin of the plant where the nectar was collected, the geographic location and the season.

Beside its use as food, antioxidant, antiinflammatory, and immune-stimulant properties have been reported, as well as cardiovascular protective and experimental antineoplastic activity.^{1,2} However, the most documented property has been as an antimicrobial adjuvant since it is known that no bacterial resistance develops, although its therapeutic use has not expanded because standardization is still lacking.^{2,3}

In foreign countries, there are therapeutic kinds of honey, used especially for the treatment of wounds.^{4,5} Several experimental studies have assessed its benefits in bisphenol A toxicity, in the healing of intestinal anastomoses, and even in the prevention of intra-abdominal adhesions due to peritonitis.⁶⁻⁸

Regarding the surgical management of intra-abdominal sepsis (IAS), wherein the main goal is eliminating the source of infection and controlling peritonitis, peritoneal lavage may be necessary; it often is a complement to well-known surgical strategies, in an attempt to eliminate bacteria from the peritoneum.⁹⁻¹² Nevertheless, certain patients will require reoperation for persistent infectious foci, failure of the surgical technique, peritoneal adhesions

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with intestinal obstruction, evisceration or surgical wound infection, among other reasons. There is a significant mortality rate, and persistent peritonitis is a feared complication in 20% to 58% of all cases of secondary peritonitis.¹³

Regarding the prognostic assessment of IAS, the Mannheim Prognostic Index is easy to use and provides useful information to assess a timely treatment option, as well as the patient's prognosis.^{14,15}

We report two clinical cases with IAS in a period from March 13 through May 18, 2016, treated on separate dates as surgical emergencies during the night shift of the Department of General Surgery at a secondary level hospital. Surgery consisted of control of the infectious source in both cases, plus peritoneal lavage in one and cavity drainage in the other. As part of the treatment and the surgical strategy, bee honey was spread in the contaminated area of the abdominal cavity, with the aim of profiting from its documented antimicrobial activity, without ignoring the potential and still unproved anti-adhesion activity, thus solving IAS in a single stage.

The purpose of reporting these cases is to create awareness on the potential use of honey in IAS, especially as an antimicrobial adjuvant.

Case report 1

This was a 53-year-old male with no relevant history. His current condition started 30 minutes before his arrival in the hospital, when he was wounded with sharp weapons and sustained blows to the abdomen and other parts of the body.

Physical examination revealed blood pressure, 90/70 mmHg; heart rate, 76 beats per minute; respiratory rate, 18 breaths per minute; temperature, 36.5 °C. The patient had apparent signs of alcoholic intoxication; he was awake, pale, with stab wounds in the frontal and parietal regions, left upper limb and left thigh, from 1 to 5 cm in length, and three abdominal wounds, i.e.: in the epigastric region and the left flank, 1 cm each, and in the umbilical region, 2 cm in length, the latter penetrating into the abdominal cavity. Multiple blunt contusions all over the body and fractured left ulna. Signs of peritoneal irritation were present,

so an exploratory laparotomy was performed. Surgical findings included: perforating wounds of the small intestine at 260, 280 and 320 cm from the angle of Treitz; perforating wound/reath of the mesentery at 290 cm; 3-mm superficial erosion of the serosa of the colon at the hepatic flexure; hemoperitoneum, approximately 500 ml, together with free intestinal content in the peritoneal cavity.

Small intestine injuries were repaired in a single-layer with non-absorbable 2-0 silk Lembert sutures; the mesenteric injury was also repaired, the cavity was cleaned, and the serosa of the hepatic flexure was reinforced. No drains were placed. Total bleeding was approximately 700 ml. The ulnar fracture was treated with a posterior splint.

Postoperative medical treatment consisted of extended spectrum antibiotics (intravenous [IV] ceftriaxone 1 g every 8 hours [h] plus IV metronidazole 500 mg IV every 8 h); IV omeprazole 40 mg every 24 h; IV lysine clonixinate 100 mg every 8 h; IV acetaminophen 1 g every 8 hours; and enoxaparin subcutaneous injection, 40 mg every 24 hours.

On the third postoperative day, 150 ml of intestinal content drained through the surgical wound. The patient looked septic, with anxious facies, pale and dehydrated; the abdomen was distended and tense.

Laboratory tests revealed: hemoglobin 12.3 g/100ml; leukocytes 14,400/mm³; platelets 186,000/mm³; PT 13.2"; PTT 22.5"; INR 0.99; glucose 201 mg/dl; creatinine 0.88 mg/dl; albumin 2.5 g/dl.

Preoperative vital signs were: heart rate, 98 beats per minute; respiratory rate, 28 breaths per minute; blood pressure, 120/70 mmHg; temperature, 36.5 °C.

Re-operation revealed a 50% dehiscence (1 cm) of the first primary repair close to the angle of Treitz, accounting for the leak of approximately 1,000 ml of intestinal content spread throughout the cavity, with thickened parietal and visceral peritoneum. Abundant fibrin, significant edema and generalized dilatation of intestinal loops were found.

An intestinal resection encompassing the three primary repairs was performed, with a termino-terminal entero-enteric one-layer anastomosis with non-resorbable material

(2-0 silk). Cavity lavage with 1,500 ml of saline solution was carried out, after which approximately 100 ml of honey were spread throughout the cavity; Penrose drains were placed in the subphrenic spaces and cul de sac. The patient was managed with an open abdomen technique using a modified Bogota bag, due to the difficulty to close the abdominal wall and the possibility of abdominal compartment syndrome. Based on the available data, the patient was graded with a Mannheim prognostic index of 25, indicating a mortality risk of up to 7%.

Postoperative evolution progressed slowly towards improvement, with early ambulation made possible by the modified Bogota bag (Figure 1). Cleaning of the surgical wound continued, including the use of honey. Total parenteral nutrition was given, together with the same extended spectrum antibiotics and symptomatic treatment as before. Feeding by mouth was started on the sixth day after re-operation. Drains were removed on the tenth postoperative day, and the Bogota bag was removed at the patient's bedside on



Figure 1. Patient with modified Bogota bag after removal of the drains.

the fifteenth postoperative day. The wound was managed as a planned ventral hernia. Considering his favorable progress, the patient was discharged 30 days after admission.

Case report 2

This was a 43-year-old female. Medical history: Allergic to penicillin and ibuprofen, umbilical hernioplasty 10 years before. Obstetric history: gravida 3, para 3, abortus 0. Date of last menses: nine days before admission.

The patient came to the emergency department with a 4-day history of lower abdominal pain. She had been treated with symptomatic medications and antibiotic (ciprofloxacin) for the first three days. The admission note stated that the patient looked pale and dehydrated, with a tense abdomen, guarding and positive rebound.

Laboratory results: hemoglobin, 9.7 g/100ml (hemoglobin on admission was 8.8 g/100ml, but packed red blood cells were transfused); leukocytes, 13,300/mm³; platelets, 529,000/mm³; PT, 1.25"; 55%, PTT 22.6", Na 138 mEq/l, K 2.8 mEq/l, Cl 111 mEq/l, glucose 78 mg/dl, creatinine 0.42 mg/dl, albumin 1.9 g/dl, total bilirubin 1.0 mg/dl, *S. typhi* H antigen 1:160, *S. typhi* O antigen 1:160, *S. paratyphi* A antigen 1:160, *S. paratyphi* B antigen, 1:160, *Brucella* 1:320, *Proteus* 1:320.

A plain abdominal X-ray revealed opacity and air-fluid levels in the lower abdomen. The ultrasound mentioned a moderate amount of free fluid in the cavity, surrounding the uterus and adnexa.

She was treated from admission with antibiotics for a presumed gynecological condition, which was ruled out by the Ob-Gyn department.

The patient was referred to the general surgery department, with the suspected diagnosis of intraabdominal sepsis (IAS). They reported the patient looked pale and dehydrated, with fever up to 38.5°C; heart rate, 108 beats per minute; respiratory rate, 29 breaths per minute; blood pressure, 100/60 mmHg. Besides peritoneal irritation, a conglomerate was palpable in the lower abdominal quadrants below the umbilicus. Management was given to improve the patient's general conditions, including a preoperative blood transfusion.

The patient underwent an exploratory laparotomy on the seventh day after her presentation to the emergency department and the eleventh day of her current condition. Surgery revealed disintegrated appendix in its proximal third, with two fecal stones in the area and a friable base; fetid fecaloid abscess of over 1,400 ml in the lower abdomen, from the umbilicus to the pelvic floor; conglomerate made up by the abscess plus omentum, loops of the small intestine and colon, uterus and adnexa, all stuck to one another and to the abdominal wall, with widespread adhesion formation.

The operation consisted of appendectomy with Parker-Kerr suture; abscess drainage and drying; adhesion removal; application of honey (approximately 100 ml) in the area of the abscess and over the released loops; and placement of Penrose drains in the cul-de-sac and the area of the abscess.

The surgical wound was left unclosed, spreading honey on the borders. Total bleeding was approximately 600 ml. The patient was graded with a Mannheim prognostic index of 27, indicating a mortality risk of up to 76.6%.

Postoperative drain output was up to 250 ml every 24 hours for 2 days, made up of cloudy, pale brown, non-fetid material that decreased gradually.

The patient was treated with extended spectrum antibiotics, as ceftriaxone, plus metronidazole. Her clinical progress was favorable. Feeding by mouth with a liquid diet was started on the fifth postoperative day. The surgical wound was cleansed and followed for secondary closure.

The patient had favorable progress and was discharged 23 days after admission.

DISCUSSION

Many therapeutic properties have been attributed to bee honey, especially its antibacterial capacity in the healing of wounds; its commercial medicinal use in some countries for this purpose leaves no doubt about its benefits.¹⁻⁵ Besides, there is a growing experimental interest in its benefits for intra-abdominal adhesions due to peritonitis.⁸

Several mechanisms have been proposed to explain honey's antibacterial activity,

including hygroscopicity that attracts humidity and dehydrates the bacteria; an acid pH (3.2 to 4.5) that inhibits bacterial growth; its contents of hydrogen peroxide produced by glucose oxidase; its contents of phytochemical factor or non-peroxide antibacterial factor; and its hyperosmolarity.^{1,2}

Nevertheless, the mechanism of action of bee honey is not clear yet, especially because of its many components, whose proportions vary between different types of honey; this leads to believe that the antimicrobial activity of the components themselves in varying proportions is synergistic.¹⁻⁵

In several parts of the world, there are already certain types of honey to which wound healing properties are attributed, such as the Tualang honey (Malaysia) and the Manuka honey (New Zealand and Australia). Some kinds are already in the market as therapeutic honey; such is the case of brands as Revamil and Medihoney.³⁻⁵

There is also information about toxic honey, obtained from plants of the *Ericaceae* family (*Rhododendron ponticum*, which produces grayanotoxin).¹⁶

Furthermore, as any natural product, honey may be subject to various types of adulteration and contamination, i.e., with pesticides, heavy metals, environmental antibiotics, microorganisms and radioactive materials.¹⁷ Bacteria and spores have been found in honey, one of the most important of which is *Clostridium botulinum*. In the aforementioned medical honeys, this is addressed with gamma rays, which do not alter their functions. Although botulism related to the ingestion of bee honey has been reported, this has only happened in infants and is considered mainly due to the lack of competitive flora in the gastrointestinal tract. Spores have not been found in all commercial honey, which suggests this finding is quite unlikely.¹⁷⁻¹⁹ Contamination with bacteria or spores could currently be a limiting factor to the widespread use of honey in the abdominal cavity, unless there is the certainty that it has been treated with gamma rays. Ideally, strict quality control and standardization are necessary in order to use honey as a medication.

Even though in many parts of the world there is no therapeutic honey, plain commercial

honey has been used and is currently used to support medical publications. Interest in scientific research on this product is growing. Reasons for such interest include the resistance of bacteria to antibiotics; the increasing number of reliable studies demonstrating the usefulness of honey; the commercial interest of the industry of honey; and the complex and unpredictable nature of this product, which poses a challenge to scientists.⁴

In cases of intra-abdominal sepsis, mortality rates may reach 30%- to 35%, in spite of preoperative medical treatment before the surgical management of the intra-abdominal source of infection; peritoneal lavage, if necessary; the use of antibiotics, total parenteral nutrition and intensive care; together with surgical management strategies such as damage control, planned versus demand relaparotomy and open abdomen, associated.^{20,21}

Furthermore, all factors involved in the morbidity and mortality in general surgery should be considered, as in any surgical specialty, since there is wide variability in surgical treatment and strategies, which together with complex IAS cases explains the outcome in each patient.

As for peritoneal lavage, attempts have been made to booster its usefulness with certain adjuvants, mainly antibiotics and antiseptics. The latter are no longer recommended, and the former perhaps cause even more adhesions;⁹⁻¹² the same happens as the number of re-operations increases.

In the two cases reported, contamination of the abdominal cavity was so severe that it entailed the risk of progression to organ dysfunction, and a dire prognosis was to be expected, associated to each patient's Mannheim prognostic index.^{14,15} In the first case, our surgery was the second that the patient underwent. Once the cause of infection was solved, peritoneal lavage was performed, and honey was spread throughout the cavity. The open abdomen technique with a Bogota bag was used, making early ambulation possible as well as the uncomplicated acceptance of feeding by mouth. The infected wound was treated with honey, and it was also used on the mesh; this increased exposure of the cavity to honey. It has been mentioned that honey may seep through

the openings in the Bogota bag by the force of gravity;²² this last fact was the reason that led us to use of honey inside the cavity.

In case 1, Penrose drains were placed in the subphrenic spaces and the cul-de-sac, anatomic sites where it is well known that free abdominal fluid collects, due to movement of the diaphragm in the former and to gravity or slanting related to the patient's position in both. The use of drains takes into account the limited anterior drainage through the modified Bogota bag in cases like ours, and especially the expected drainage of honey and detritus or possible leaks, which did not happen in our patient.

In the second case, a modified clinical picture was encountered; an early diagnosis was not established, which is crucial to reduce morbidity and mortality in patients with IAS. And even though peritonitis was not generalized, it involved all the lower abdomen, with purulent material of fecal origin collecting for over 11 days, which led the peritoneum to a severe level of contamination. It was highly possible that the patient would require relaparotomy, so honey was left inside the abdominal cavity in an attempt to prevent it. A score of 27 in the Mannheim prognostic index led us to use honey in this patient. Drains were placed in the large contaminated area with the same purpose as in the previous case, and their usefulness was apparent.

The placement of prophylactic drains is a very controversial issue, and the available evidence-based information is not yet definitive to rule out their usefulness, especially in cases of IAS as complex as these. This information should serve as a guide for our judgment in treating each particular patient.^{23,24}

The honey we used was a commercial brand that is recommended for complying with its properties, according to quality studies carried out by the Federal Consumer Protection Agency (Profeco).

In each case, the amount widely distributed throughout the abdominal cavity in the first case and in the lower abdomen in the second case was less than 100 ml in each. This is explained by the dilution that honey undergoes when it is spread and comes into contact with the fluids inside the cavity. Later on, it pours out through the drains together with other secretions, but

given the recumbent position of patients in the postoperative period, honey came into contact with all the abdominal contents for a certain time.

Favorable clinical evolution of both patients was due to a number of factors. Besides the main goal, which was treating the cause of infection in both cases and following procedures with a proven usefulness, such as peritoneal lavage and the open abdomen technique, honey was applied inside the contaminated abdominal cavity as an adjuvant. The above is supported by literature that demonstrates the documented antibacterial activity of bee honey, plus its potential to prevent peritoneal adhesions, in addition to the observed and accumulated experience in the management of infected wounds in patients using the modified Bogota bag.²² Furthermore, with the aim of preventing persistent peritonitis, and pursuant to Title 5, article 103 of the General Health Law, since the two cases were considered an emergency, were seen on different dates and were treated during the night shift of our department, they were not preoperatively assessed by the Ethics and Research Committee. However, this should provide the basis to develop research protocols on the use of bee honey in IAS.

CONCLUSIONS

Based on the available information about honey, benefits in IAS may be expected, since its antimicrobial activity looks promising. Although recognizing its limitations, honey could be an adjuvant to therapeutic interventions or surgical approaches when necessary. Further studies could clarify these points. Besides, in order for it to be used as therapy in the future, each type of honey should be standardized and subject to quality control.

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