BIOSURGERY THE FUTURE OF NON HEALING WOUNDS

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As our society is ageing the number of patients suffering from chronic wounds arising from diabetes and peripheral vascular disease is constantly growing. It places an enormous burden on our health care system. Chronic wounds require long-term treatment, what results in the increasingly higher costs. Biosurgery, as an alternative to a classic wound dressing, proved to be a very effective and quick method of wound cleansing. It hastens the healing process, and hence lowers the overall cost of the treatment (1). It uses sterile maggots Lucilia sericata. The simplicity and limited number of side effects makes it a very promising method of chronic wound dressing. This article aims to present a current practical and theoretical understanding of biosurgery.

History

The history of biosurgery dates back to the times of native tribes of New South Wales, Burmese highlanders as well as ancient Maya people. The first physician to observed a positive influence of maggots on the process of chronic wounds healing was a French surgeon, Ambroise Paré (1510-1590). The turning point of his experience with biosurgery was during an observation of a patient with a severe head wound, where maggots significantly contributed to the recovery. Thereafter Paré allowed maggots to live in the open wounds, as a factor enhancing healing process. The first documented example of applying maggots at an open wound was a publication by a military physician, Forney Zacharias (1837-1901), who described it during The Civil War. A real breakthrough however transpired in 1928, when William Baer, an American orthopedist from John Hopkins University applied facultative parasitism principles in a bone inflammation treatment of four children. In those days the therapy was deemed the quickest and the most effective method of bone inflammation treatment. In the thirties over three hundred American hospitals were using biosurgery as a standard in chronic wounds treatment, and over one hundred papers were published on the subject. However, an advent of sulfonamides and industrial technology of penicillin production in the forties ousted biosurgery from the health care. Present renaissance of the method is caused by a growing antibiotic resistance and constantly increasing cost of the chronic wounds treatment.

A significant contribution to the revival of biosurgery is attributed to Ronald Sherman, employee of the University of California Irvine Medicine School, USA. Together with his co-worker, he conducted research that helped biosurgery back to the academic medicine. In 1996 International Biotherapy Society, an entity examining role of the living organisms in the wound healing process, was established.

Nowadays, utilization of maggots Lucilia sericata for healing purposes is getting a growing number of supporters. The comeback of maggots therapy is an effect of a progressive ageing of the society. This demographic transformation prompts the increase of illnesses causing intractable wounds, and in effect imposes heavy costs on the overloaded health care system (2-6).
Mechanics

Cornerstone of the intractable wounds treatment is a proper debridement, sustaining moist environment and preventing infection. Using maggots in the treatment helps to change the course of healing from chronic to severe (normal wound healing phases)(7). During the process maggots devour bacteria along with liquid dead tissue, and subsequently bacteria are destroyed within their digestive system. The whole process is so efficient, that maggots are able to change the wound from rank and infected to clean and healthy within just few days. Numerous authors divide the mechanics into three stages: debridement, disinfection and stimulation of healing.

Debridement

Debridement is a stage thanks to which we gain control over an inflammation, limit bad odour and expose healthy vascularized tissue. Biosurgery enables debridement on the microscopic level, with minimal damage to a healthy tissue – the quality that gives biosurgery an upper hand over traditional methods. Maggots Lucilia sericata are necrophagous organisms feeding on dead tissue and ooze coming from the wound (3). As an organism, maggot is devoid of teeth, and hence digest extracorporealy by secreting a number of enzymes including: carboxypeptidases A and B, leucine aminopeptidase, collagenase and serine proteases (trypsin-like and chymotripsin-like), aspartyl proteinase and metalloproteinase (8). Digested tissue is subsequently painlessly consumed by the maggot. One maggot consume approximately 0.15 gram of dead tissue a day. Depending on the number of maggots used and the time over which the dressing is applied, it enables to clean the wound to a substantial extent (9). Approximately 5 to 10 maggots a cm² is suggested (10).

Disinfection

Apprehension of the mechanics by which maggots can bring infection under control in scope of the wound was altering alongside the development of the research methods. The first theory implied that maggots activity intensify the oozing, and hence cause mechanical rinsing of the wound. Rich with proteolytic enzymes ooze was supposed to contribute to digestion of bacteria. It was also proved that bacteria consumed by the maggot die in its digestive system. Excreting ammoniac and calcium carbonate, maggots increase pH index of the wound, what constrains expansion of the bacteria and broadens an activity of the proteolytic enzymes (6, 8, 11). The antiseptic mechanics is not completely intelligible. Due to the ambiguous results of the research, the direct antiseptic in vitro effect could not be proved (12). Nevertheless, presence of at least two active antiseptic agents, characterized by a broad spectrum of activity G(+), G(-) including MRSA, has been proved. Modern methods of isolation allowed approximate stipulation of the antiseptic substances nature as thermostable and protease resistant (size <500 Da and 0.5-3-kDa) (13, 14, 15). Last researches indicate that maggots play a key role in breaking bacterial biofilm with Pseudomonas aeruginosa, what additionally promotes its usage for infected wounds (16).

Stimulation of healing

Maggots stimulate healing by draining a tissue, what enables better access to oxygen and enzymes. They excrete allantoin and urea, which are ingredients of numerous healing ointments (6). Experimental tests confirmed that maggots' excretions/secretions (ES) causes increased activeness of fibroblasts in vitro (17, 18, 19), and also inhibits pro-inflammatory function of neutrophiles (20) and monocytes (21), without suppressing phagocytosis. Described was also immuno-moduling effect based on decreasing the production of TNF-α, IL-12p40 (pro-inflammatory function) and increasing IL-10 (anti-inflammatory function). The latest research enabled isolation of IFN-gamma and beta-FGF from the ES maggots. Those agents have a fundamental role in philological healing processes (19). Wang and assoc. showed that ES induces human microvascular endothelial cell migration through AKT1 (22). Moreover, authors are unanimous regarding its beneficial effect on wound remodeling.

Indications and contraindications for biosurgical debridement

Biosurgery is very effective with intractable wounds. Physicians all over the world use this
method especially willingly with diabetic wounds and other wounds with large amount of dead tissue, and get good clinical results (23-28). Some the applications of "living wound dressings" described in the literature (6) are as follows:

- diabetic ulcers,
- ulceration (venous, arterial, venous-arterial, naturopathic),
- pressure sores,
- thromboangiitis obliterans,
- tumour-related wounds,
- necrotizing fasciitis,
- pyoderma gangrenosum,
- osteomyelitis,
- burns,
- severe wounds,
- mastoiditis,
- pilonidal sinus,
- wound infected after breast operation,
- wounds after a knee joint endoprosthesis,
- non-healing wounds after surgeries,
- MRSA infected wounds,
- condition after removing medial malleolus abscess,
- infected gun shot wound.

A few of them were not long ago disadvised, due to a problematic location of the dressing (what caused difficulties during disposal of maggots). This includes: cleansing of peritoneal cavity, glans penis or pleural space (29). Immuno-modulating mechanics described above justify treatment of pyoderma gangrenosum and other skin alterations with autoimmunologic background. Another thesis emphasize antiseptic property of maggots which contribute to good clinical results in infected wounds dressing MRSA (14). Another extremely important aspect is a tumour-related wounds treatment, where cleansing has a palliative character. It helps to eliminate an unpleasant odour, which is often embarrassing for a patient. Nowadays maggots are more willingly used for non-chronic severe wounds (29). Relative contraindications include dry wounds (maggots require humid environment), opening abdominal cavity and neighborhood of large blood vessels (Difficult disposal of maggots). There is also one strict contraindication – allergy to maggots (6).

Side effects

Biosurgery therapy is considerably safe and entails few possible side effects. One of the most dangerous is an infection transmitted by non-sterile maggots. However, ensuring proper breeding conditions and sterility minimize the problem considerably (30). In case of large amount of dead tissue a disagreeable odor caused by engaging the wound is likely, but this can be mostly eliminated after first change of dressing. Very important factor is a technique and thoroughness of dressing application, as it determines the stability of dressing and prevent maggots from getting out, what could discourage patients and medical personnel alike from using the therapy. Pain rarely accompany the therapy and is easily subjected to pharmacotherapy (31, 32). Mentions about bleeding from biosurgeryaly cleansed wound seldom occur (33).

Biosurgeryal dressing

Correctly applied dressing is a significant element of the biosurgery therapy. Its main purpose is to keep maggots within the limits of the wound. It has to be thigh enough lest “little surgeons” escape, and airy enough to enable them their work. During the process of debridement wound usually become more soggy and oozy, hence extra gauze should be applied. Biosurgeryal dressing should be applied for approximately 3-4 days. However, it is not possible to stipulate the exact time, as it is individually tailored to each patient. A good yardstick is a size of maggots. While applying, they are the size of a rice grain, and provided the debridement proceeds successfully, they grow 1 cm long. Varied techniques of “living dressing” application, depending on the location of the wound, are available. They all consist in constructing a “cage” which restrict maggots to the area of the wound. There is an alternative dressing called Biofoam, in which sterile maggots are mixed up with scraps of foam and put into a handy bag, what keeps them out of sight. Cage dressing is cheaper and more available than biofoam, and being equally effective, it is more frequently in use(9). General rules of cage dressing preparation boils down to four simple steps, which are:

I. Covering healthy skin → II. Applying maggots → III. Securing maggots with cage → IV. Applying outer dressing.

It must be remembered that biosurgeryal dressing, by virtue of its living nature, requires
exceptional precautions. Wetting, drying or squashing is strongly disadvised as it can disturb the debridement (30, 31).

**Costs**

Economic aspect of biosurgery was comprehensively described in British conditions. Among the publications we can find calculations unambiguously in favour of biosurgery, as well as those regarding it financially comparable with classic therapy. Wayman and assoc. presented result ranging from £79 to £136, whereas Thomas and assoc. put it between £82 and £503 (adding up nursing care cost) respectively for patients treating with biosurgical and classic dressing (34, 35). Dumville and assoc. indicated that the time of wound debridement was considerably shortened, but it didn’t entail lower cost of the therapy (36). As for polish conditions, breeding of sterile maggots Lucilia sericata is getting more and more common, what entails its market price drop. Appearance of local sellers has broken the barrier of expensive import. Some of the authors encourage hospitals to breed maggots independently in specially appointed spaces, what should additionally lower costs of the therapy (37).

**DISCUSSION**

Nowadays, maggots are used in hospital as well as ambulatory treatment all over the world. Researchers form prestigious R&D centres publish another papers confirming the relevancy of biosurgery. Moreover, there are reports indicating new and broader applications of the therapy. According to present knowledge biosurgery is a good form of intractable wounds treatment. It is characterized by efficient wound debridement, safety, simple usage and low cost. Possible problems with implementation of presented therapy most probably result from epidemiologic reasons. Physicians of different specializations on many occasions had to do with “quasi biosurgery”, when treating extremely neglected patients. Unfortunately there is an abundance of mentioned cases, what definitely poses a barrier for practical application of maggots in medical treatment. Another hindrance is a limited availability of good quality local maggots breeding centres, what gives no alternative for imported material, and has an ill effect on economic side of the therapy. Mentioned by numerous authors “yuck factor” seems to be of no significance after appropriate acquaintance of patient and personnel with the method. Hopefully, as time passes, “quasi surgery” will become history, replaced by modern and acceptable form of chronic wound treatment. It is expected, that the number of high quality national maggots breeding centres will constantly grow, and hence biosurgical therapy will become naturally and commonly worthwhile form of a chronic wound treatment.

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