

## Argentum–quarz solution in the treatment of anorectal fistulas: Is it possible a conservative approach?

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### ABSTRACT

Patients suffering from chronic intestinal diseases (Crohn's disease, Ulcerative Colitis, Indeterminate Colitis) are prone to the development of pyogenic complications. These complications are most commonly in the form of perianal or intraabdominal abscesses and/or fistulas. The treatment of these complications are managed differently but, after an initial treatment based on medical or minimally invasive management, the solution of the pathological condition is always achieved by a surgical procedure.

In the last few years prospective studies have proposed an alternative conservative therapeutic approach based on application of fibrin glue in the healing of patients with fistulas-in-ano.

In this paper we suggest and discuss the therapeutic potential of silver and quartz in the conservative treatment of anorectal fistulas pointing out their role in modulating particular steps of the pathogenetic process which characterizes this pathological condition.

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### Introduction

The anal fistulas are acute or chronic suppuration caused by an infection of a gland localized in the Lieberkuhn crypts at the level of the rectum and anal canal. The contact of enteropathogenic bacteria with the mucosa of the crypts, associated with other competing situations (inflammation of the mucosa, constipation), can cause and abscess due to penetration of pyogenic organisms in the tissue-sphincter. Hence the abscess diffuses into the peri-rectal cell-areolar tissue, spreading in adjacent spaces towards perianal skin, after passing through the sphincter apparatus. In addition to infection of a gland at the level of intestinal crypts, another cause of anorectal fistula formation may be the presence of chronic intestinal diseases such as Crohn's disease, Ulcerative Colitis and Indeterminate Colitis. In all cases, the symptoms consist of an inflammation in the site of formation of the fistula, associated with pain and difficulty in defecation. Currently the treatment of fistulas

requires a surgical approach, aimed to total and accurate removal with different techniques, chosen according to the type of fistula, site of formation, and the specific type of involvement of the sphincter apparatus.

As an alternative to the surgical procedure, a less invasive approach, which involves the injection of fibrin glue or the use of collagen plugs, begins to develop [1–3]. Interestingly it has also been reported the use of silver preparations in the treatment of tracheo-bronchial fistulas [4,5].

### Hypothesis

As aforementioned the pathogenesis of anorectal fistulas involves an inflammation process caused by enteropathogenic bacteria whose persistence is probably the main reason of the impossibility of healing of the lesion [6].

Intriguingly, published data [7,8] reported that silver-based medical preparations exert both an antimicrobial effect and a role in attenuating the inflammation of the airway in a murine model of asthma [9]. Furthermore both silver-based preparation and quartz can modulate the proliferation rate of fibroblast cells which are the main actors of wound healing process [10,11].

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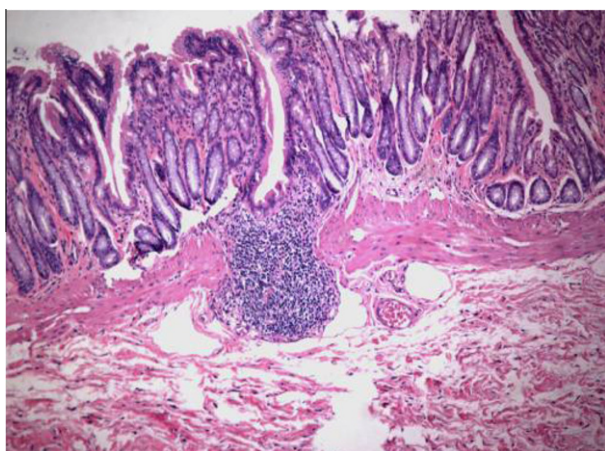
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In light of the aforementioned published data we suggest that anorectal fistulas can be treated in a conservative manner by means of a topic administration of an “argentum–quarz solution” which might contribute to the healing of the lesions through its antimicrobial activity but also modulating the proliferation and differentiation of fibroblast cells.

### Evaluation of hypothesis and discussion

Chronic wounds, as anorectal fistulas infected by enteropathogenic bacteria, show individual combinations of causes leading to the impossibility of a repair and difficulties in standardizing a common care for all patients. The main feature of chronic wounds is the persistence of an inflammatory status characterized by a continuing influx of neutrophils that release cytotoxic enzymes, free oxygen radicals, and inflammatory mediators that cause extensive collateral damage to the tissue. In our opinion, it is reasonable to speculate that within an anorectal fistula healing and destructive processes are out of balance and consequently, by manipulating and counterbalancing these processes, the chronic wound might start to heal. In this regard we think that a solution based on silver and quartz could be a promising therapeutic option. Silver, indeed, could negatively modulate the proliferation of fibroblasts counteracting the infectious action of pyogenic bacteria but, in synergism with quartz, could also stimulate proliferation and differentiation of fibroblasts into myofibroblasts leading to a resolution of the problem [12]; this second effect is probably due to the ability of silver to cause a certain cytotoxicity as we observed an inflammatory infiltration after administration on murine perianal mucosa of an “argentum–quarz solution” (Fig. 1). In particular the perianal mucosa was taken under sedation (Tiletamin + Zolazepan 50 mg/kg i.m. + Medetomidina 50 mcg/kg i.m.) and orotracheal intubation (FiO<sub>2</sub> 50%, air 50%, isoflurane 3%).

In favor of our arguments we report at least two works which pointed out that silver nanoparticles can both cooperate with antibiotics [13] in bactericidal action and improve the tensile properties of the healed skin through a better collagen fibril alignments [14]. In particular Fayaz et al. proposed a mechanism to explain the synergism between silver nanoparticles and ampicillin consisting of their ability to form a core with the antibiotic able to inhibit both the formation of cross-links in the peptidoglycan layer (leading to cell lysis) and the DNA unwinding. Furthermore, in a wound healing murine model, it has been shown that topical delivery of silver nanoparticles was able to reduce the levels of acute-phase



**Fig. 1.** Histological analysis of a region of perianal mucosa treated with an argentum quartz solution. An inflammatory infiltration (monocytes) takes origin from submucosa tunica and reaches up to mucosa tunica.

proteins as hemopexin (Hpx), haptoglobin (Hpg), and serum amyloid protein component P (SAP) [15].

### Conclusions

The correct repair of a lesion with the “restitutio ad integrum” is a complex process in which inflammation plays a dual role: it indeed, through molecular pathways dependent on proinflammatory cytokines, lead to differentiation of fibroblasts into myofibroblasts with a reparative action [16], but when inflammation persists for a long period becoming chronic the outcome is the process of fibrosis which compromises the normal function of the tissue.

In the case of anorectal fistulas a chronic inflammation could arise because of the presence of enteropathogenic bacteria, so the main therapeutic approach should be directed against this problem. On the other hand inflammation is important to stimulate the repair process consisting of stimulation of proliferation and differentiation of fibroblasts.

We propose that an “argentum–quarz solution”, based on silver and quartz, could be a useful, non surgical, therapeutic approach to treat anorectal fistulas because of the aforementioned ability of silver and quartz to reduce bacterial infection but also to modulate proliferation and differentiation of fibroblasts.

### Conflict of interest statement

None declared.

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