

Benefits of crenotherapy in digestive tract pathology (Review)

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Abstract. Balneotherapy, a branch of physical and rehabilitation medicine using the natural factors of balneal resorts for therapeutical purposes to modulate the symptoms of numerous diseases, represents a non-pharmaceutical therapeutic alternative, easily accepted by patients and used both preventively and curatively. Crenotherapy, a branch of balneotherapy, is the method in which mineral waters are used as a therapeutic internal cure by ingestion. This procedure is performed in spa resorts (where these natural resources exist), and the ingestion of mineral water takes place at the source (spring), in the quantities recommended by the medical rehabilitation physician, according to specific regimens for the condition to be treated. Depending on their physical and chemical composition, the therapeutic mineral waters fall into several categories, having clear indications for certain pathologies. Hypotonic, isotonic, or slightly hypertonic mineral waters are recommended in diseases of the digestive tract and hepatobiliary conditions. Over time, studies have been conducted to determine the effect of these types of treatments, highlighting the complex influence of crenotherapy on the gastrointestinal tract, with favorable

results, therefore the use of mineral water intake in various pathologies being recommended. The current review focuses on the existing literature data and refers to the main progress made in understanding the benefit, indications, and crenotherapy procedures in the management of gastrointestinal disorders.

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1. Introduction

As therapeutic tools, mineral waters are most frequently used as internal cure (crenotherapy) and also in the external cure, using various individualized techniques based on the type and stage of the disease or based on the patient's response and co-morbidities (1).

In Antiquity, on the Dacian territories, the Geto-Dacian population founded settlements in the vicinity of the natural springs (Utidava, Petrodava), which were used for therapeutic purposes, upon the indications of the priests. There are documents attesting that 2500 years ago, Herodotus recommended the 21-day cure of mineral water, a fact scientifically confirmed only in the twentieth century (2).

Over time, many digestive pathologies have been referred to obtain the beneficial effect of crenotherapy; even the term and the beneficial link were later defined. The impact on the digestion pathways, on the peristalsis, or the potential antiseptic effect of some mineral waters raised the interest for improving different pathological situations (3). Physicians are already trying to add their possible effects to current pharmacologic or surgical treatments, considering that balneal treatments can

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provide a noninvasive way that can improve the quality of life in many cases (4).

In 1924, in Bucharest, A. Teoharia was the first researcher preoccupied with the physicochemical properties of mineral waters and their benefits on human health. This research was later published in 1929 in *Somes Archive* by the writer Virgil Sotropa, which presents the popularity of these natural resources in different pathologies, including gastritis and bile or liver diseases (5). During the second half of the twentieth century, the therapeutic effects of mineral waters of Romania were scientifically confirmed, some of them being recommended for use as crenotherapy of digestive and hepatobiliary tract diseases (6).

Most countries benefitting from natural springs of mineral waters have undertaken research in terms of the physicochemical composition and also on the effects of mineral waters, identifying the uses of various types of mineral water for specific pathologies. In 2009, a centralized classification of mineral waters was performed, according to European legislation (1). Thus, the main categories are bicarbonate-rich, sulphurous, chloride, high-calcium, high-magnesium, fluoridated, and ferruginous (chalybeate) mineral waters (1,7).

Mineral waters, based on biological activity, can be classified as: cathartic waters, diuretic waters and waters with antiphlogistic properties (8).

This article reviews the clinical studies conducted in the last five years on the effect of mineral waters in gastrointestinal disorders, using data from the MEDSCAPE and PubMed portals; 9 eligible studies were identified (Table I).

2. Pathogenic background for crenotherapy usage

There are certain chronic diseases of the digestive and hepatobiliary tract, for which spa treatment, including crenotherapy with mineral waters, can contribute to a better result, by complementing the effects of basic dietary, pharmacological and surgical therapies. The mineral waters used in the internal cure represent, in fact, a non-pharmacological therapy, considering the natural, albeit pharmacological resource, based on their chemical content.

Thus, depending on their composition, there are indications of therapeutic cures in which simple alkaline or bicarbonate waters are used. These contain at least 1 g of salts/liter, with the predominance of bicarbonate ion bound to Na and K cations. The effects of these waters on the digestive tract reside in the action of Na/K bicarbonate, an alkaline substance, confirmed by studies carried out by specialists from spas and the National Institute for Rehabilitation, Physical Medicine, and Balneology (1,5,9). The ingestion of these waters reduces the chlorhidropeptic secretion (when ingested an hour and a half before a meal) or stimulates it (administered during a meal), also affecting gastric motility and bile ducts, such as fluidization of the bile, depending on the method of administration. In Romania we provide this treatments in Slanic Moldova and Sangeorz Bai balneary resorts (1,6,9).

Another category, alkaline-earth sodium bicarbonate, high-calcium, and high-magnesium waters have an excitation effect on gastric secretion (Calimanesti-Caciulata, Slanic Moldova) through the predominance of CO₂, NaCl, H₂S, or sulfates (1,5).

Sulfurous waters (Baile Olanesti, Calimanesti-Caciulata, Mangalia, Herculane) stimulate gastric secretion, are choleretic, cholecystokinetic, gastric, and intestinal motor stimuli. Hydrogen sulfide regulates the function of biological systems and plays a vital role in various systems and diseases (9).

The hydrogen sulfide present in these waters is responsible for the stimulating effect on the enzymatic and metabolic processes in the gastrointestinal mucosa, stimulating the chemoreceptors, a fact that has been experimentally confirmed (1,7,9-11). Depending on the chemical composition of different sulfur waters, their effect on the digestive tract is different, as follows: poorly mineralized sulfur waters (Mangalia, Baile Olanesti springs 10 and 24) stimulate gastric secretion initially, a stimulation followed by an inhibition phase; those from Caciulata spring 1 (one) and Calimanesti spring Pausa 1 and 2 have a stimulating effect on the gastric secretion, those from Calimanesti spring 1 stimulate secretion after an initial phase of inhibition, and those from Baile Olanesti springs 5, 7 and 12 inhibit secretion (1).

Oligoelements play essential roles in the metabolism and function of the gastrointestinal and renal tract (12). In sodium, magnesium, and calcium sulfate waters, the effects are choleretic, cholecystokinetic and laxative (Amara, Baltatesti, Nicolina-Iasi). Mineral calcium and magnesium sulfate waters are confirmed to have a hypoglycemic and lipid-lowering action. They may be used as alternative therapeutic approaches of metabolic syndrome and mild forms of diabetes mellitus, preventing progression to disabling complications, such as diabetic retinopathy of diabetic foot (13,14). The effects on the secretion of the stomach are different, depending on the complexity of the chemical composition: the water from Amara decreases gastric secretion. At the same time, that of Bizusa spring 1 intensely increases the secretion and acidity of gastric juice (1,5).

Chlorosodium waters used as internal treatment are hypotonic or isotonic waters, with concentrations below 10 g Na Cl/liter. These stimulate gastric and intestinal secretion, activating digestive enzymes (pancreatic-intestinal amylase), increasing gastrointestinal peristalsis reflexively, the elements present in these waters stimulating the vagus nerve (1,6,9).

The indications regarding the dosage and the administration method are individualized and depend on the patient's condition and the experience of the physician (5). The choleretic effect is helpful in biliary dyskinesia but must be used with caution in patients with biliary microlithiasis, being a possible trigger for calculous migration and cistic or common bile duct (CBD) obstruction, responsible for acute cholecystitis and angiocholitis, which requires rapid surgical treatment (15,16). The potential harmful effects of sulfate waters may lead to increased transaminases in vulnerable subjects, thus is contraindicated in patients with hepatitis (17). The comprehensive medical history and the complete clinical evaluation of the patient before crenotherapy indication are imperative. The benefits, the potential side effects, and therapeutic alternatives should be considered before its initiation (18).

The integrity and functioning of the gut microbiota can be influenced by infections, medicine/food supplements and preservatives. Hydrogen sulphide, in optimal concentrations,

Table I. Clinical studies conducted in the last five years on the effect of mineral waters in gastrointestinal disorders.

Authors	Country	Year	No. of patients	(Refs.)
Dupont <i>et al</i>	France	2014	244	(27)
Bothe <i>et al</i>	Slovenia	2015	106	(28)
Naumann <i>et al</i>	Germany	2016	100	(29)
Quattrini <i>et al</i>	Italy	2017	Not mentioned	(25)
NIH, ClinicalTrials.gov	France	2017	166	(30)
Dupont <i>et al</i>	France	2019	226	(31)
Dragomiretska <i>et al</i>	Ukraine	2020	90	(32)
Constantino <i>et al</i>	Italy	2020	Not mentioned	(33)
Chavez <i>et al</i>	Brazil	2020	50	(34)

protects the gut flora from the lesions caused by these stressors, stimulate the resorption of the inflammation and cure local wounds (19,20). The H₂S concentration in healthy adults varies between 0.3-3.4 mmol/l (19), the higher concentrations being able to cause injury to the intestinal microbiome, disturbing the processes in which it is involved (21,22).

In current practice, sulphurous waters with concentration below 20 mg/l are used as an internal cure, because H₂S has anti-diabetic effects, anti-oxidant properties and antiaging effects, as it inhibits the DNA alteration (23,24).

Alkaline water also results in a decrease in cardio-vascular risks, reducing morbidity and mortality in the elderly population presenting comorbidities (25).

The sulphurous mineral waters above this concentration of 20 mg/l are only used as external cures (for instance, Pucioasa waters of 1,152 mg/l). In addition, the quantity of water used in sulphurous water crenotherapy is small, 50-100 ml/day up to a maximum of 400 ml/day (1).

Alkaline water having a minimum of 1 g of salts/liter with a preponderance of the bicarbonate ion and a pH above 7.0, has proven health-promoting benefits, leading to an equalization of the pH of the entire body (26).

The main diseases of the digestive tract treated by crenotherapy are gastro-duodenal dyspepsia, chronic gastritis, duodenitis, gastric or duodenal ulcer, sequelae after surgery, idiopathic gastric dyspepsia, chronic, nonspecific enterocolopathy, chronic constipation, unidentified digestive disorders due to irrational alimentation and stressful conditions (1,9,17).

Although crenotherapy is widespread, the current literature lacks evidence-based data including any exact classification of the different types of mineral waters that can be used as a general guide for the balneology practitioner, or therapeutic protocols available. There is not yet a defined global consensus regarding the indications, therapeutic programs, and their application; all of these differing from one country to another and from one spa to another in terms of crenotherapy. Currently, no international agreements have been established for this type of therapy (10). Romania remains one of the countries with a great variety of natural therapeutic resources, holding 30% of Europe's supplies. In addition, the richness of spas (160) renders Romania a vital pillar in the development of spa tourism (1,5,6).

3. Evidence-based literature data focused on the benefit of crenotherapy for GI (gastrointestinal) tract pathologies

Our review intended to expose the current evidence-based clinical benefit of crenotherapy in gastrointestinal (GI) diseases by analyzing the research reported between 2015 and 2020 on Medline or PubMed online database.

Low functional transit or functional constipation, one of the most common symptoms related to the GI tract, especially in women, has been an issue of crenotherapy indication. Dupont *et al* demonstrated in a double-blind, randomized, placebo-controlled study on 244 women from France the benefit of crenotherapy with intensely mineralized water rich in magnesium and sulfates in the alleviation of functional constipation during the second week of treatment. The researchers also affirmed a significant decrease in the need for laxative drug use after the same interval (27). Another similar placebo-controlled, double-blind study conducted on 106 patients suffering from functional constipation published by Bothe *et al* evaluated the efficacy and safety of magnesium and sulfate-rich mineral waters on gut function. The results indicated improved intestinal peristalsis and stool consistency, as well as increased quality of life for patients consuming 300-500 ml of mineral water for six weeks (28).

Naumann *et al* published in 2016 'Forshende Komplementarmedizin', a double-blind, randomized, placebo-controlled study on the effects of richly mineralized sulfurous water consumed daily for six weeks, and compared the impact to that of carbonated water consumption in a control group. The efficacy of the treatment was observed after three weeks from the baseline by increasing the intestinal motility in the experimental group (2.02±2.22 bowel movements per week) as compared to the control group (0.88±1.67 bowel movements per week) (29).

In 2017, Quattrini *et al* published an article on the effects of natural mineral waters on health, depending on their physico-chemical characteristics. The study conclusions indicated that bicarbonate mineral water neutralizes gastric acid secretion, increasing the pH of the gastric lumen, stimulating the release of digestive hormones. Chlorinated mineral water stimulates gastric emptying and gastroduodenal peristalsis; the magnesium waters relieve constipation, reducing the associated symptoms. In addition, the functionality of the biliary tract is

improved by complex mineral waters such as sulfurous-bicarbonate-calcium-magnesium-rich water, due to the anions with choleretic and cholagogue function and the high-magnesium waters favor the relaxation of the Oddi sphincter, allowing the bile to drain, thus improving the activity of the biliary tract (25).

Another ongoing interventional clinical trial, initiated by Bourgeois in 2017, published partial results on the prophylactic effect of rich magnesium mineral water over the hypomagnesemia induced by anti-epidermal growth factor receptor (EGFR) monoclonal antibodies, indicating a decrease in the incidence of hypomagnesemia as a side effect in such patients. The research was performed on 166 patients undergoing treatment with anti-EGFR monoclonal antibodies for different neoplasia (metastatic colorectal cancer or head and neck cancer), associated with ingestion of mineral water rich in magnesium and poor in sulfates. The mineral water used in this research (Rozana-France) has the highest concentration of magnesium (160 mg/liter) and the lowest sulfate content (30).

Later, in 2019, Dupont *et al* published a multicenter, double-blind, randomized, controlled study concerning the immediate effect of crenotherapy with magnesium and sulfurous mineral water in functional constipation, confirming the effectiveness and safety of the mineral water use as a first-line curative procedure. The studied patients consumed 1.5 liters/day of Hepar mineral water (France) for 14 days. Researchers confirmed that the mean duration of treatment to obtain constipation relief was shorter in the Hepar mineral water experimental group than in the control group (6.4 vs. 7.3 days, $P > 0.05$) (31).

In 2020, Dragomiretska *et al* published a study in which 90 patients from Ukraine were divided into three equal arms according to the main treatment: i) pharmacologically with proton pump inhibitor, ii) bicarbonate mineral water, and iii) magnesium sulfur bicarbonate mineral water. The results indicated the highest efficacy on dyspepsia and pain syndrome of treatment applied in the third group (32).

Other literature data referring to the effects of magnesium-sulfur mineral waters on functional constipation concluded that mineral waters such as Hepar (France), Ensinger Schiller Quelle-ESQ (Germany), and Donat Mg (Slovenia) represent a natural option for treatment in functional constipation, having a laxative effect, without noticeable side effects (9,32). The authors recommend the daily magnesium consumption of at least 20 mM for a minimum of one week to obtain the mentioned effects (32).

Another article published by Constantino *et al* in 2020 focused on sulfurous water as a medical resource in certain diseases. The authors concluded that daily ingestion of sulfurous-magnesium mineral water increased gastric secretion and stimulated its evacuation, modulating the motility and releasing the substances accompanying the digesting process (33).

In 2020, a recent study made by Chavez *et al* highlighted the effects of crenotherapy with alkaline water (pH=8.0-10.0) administered for five months for gastritis symptom relief. The results showed that besides the beneficial effect of crenotherapy with alkaline water on gastritis symptoms, an improvement in the RNA expression was present, the alkaline water intake

significantly increasing the expression of various genes related to the digestion process (34).

4. Conclusions

Natural mineral waters represent a valuable therapeutic resource in some circumstances, representing an alternative to pharmacological treatment or an adjuvant, relieving the symptoms of gastrointestinal diseases and increasing the quality of life. According to their composition, therapeutic mineral waters are recommended for consumption as an internal cure in both physiological and pathological conditions, allowing a decrease in drug consumption or the reduction of doses used in classical treatment regimens. Further research focusing on the benefit of crenotherapy is expected, literature being insufficient especially in regards to functional and organic digestive diseases.

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Availability of data and materials

All information found in this review is documented by relevant references.

Authors' contributions

AIS, LM, MD and AdPS conceived and designed the review. FV, AnPS and SIM acquired the data. MGI, AnPS and CV analyzed the data. AIS, FV and SIM validated the results. LM, MGI and AdPS were responsible for the preparation of the original draft. AIS, LM, MR and AnPS were responsible for the final manuscript editing. AdPS, LM and CV supervised the manuscript publication. SIM, CV, AIS and FV revised and made all the corrections required for final manuscript publication. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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