



Fondazione per la Ricerca Scientifica Termale

2011

SALUTO DEL PRESIDENTE



siamo ormai alla III edizione di questa brochure e ho ritenuto doveroso, oltretché un grande piacere, rivolgere un caloroso ringraziamento a Federterme e a tutti gli imprenditori termali che hanno fortemente voluto questa Fondazione e stanno contribuendo alla sua affermazione.

E' infatti grazie al loro apporto che le acque minerali termali, le cui virtù terapeutiche erano apprezzate fin dai tempi dell'antica Roma, sono divenute in epoca moderna oggetto di particolare attenzione anche da parte degli Organi istituzionali e di Governo, che hanno espressamente richiesto al mondo termale lo sforzo di validare un'antica e consolidata tradizione con studi scientifici da realizzare secondo i più rigorosi standard di ricerca a livello internazionale.

Pertanto, anche nel rispondere a tale sollecitazione, la Fondazione ha dato impulso alla propria attività di granting, che, solo nell'ultimo triennio, ha prodotto risultati che non esitiamo a ritenere soddisfacenti e dei quali vogliamo rendervi partecipi: 53 progetti di ricerca pervenuti, 30 quelli finanziati per un totale di 2,5 milioni di euro complessivamente stanziati; 23 i lavori pubblicati su riviste scientifiche ISI-PubMed con fattore d'impatto. Circa 20 gli enti di ricerca proponenti e più di 30 gli stabilimenti termali che hanno messo a disposizione oltre alla materia prima anche il proprio know-how. Questi risultati sono anche il frutto dell'adozione di una moderna piattaforma web di standard internazionale.

La Fondazione ha l'onore di collaborare con l'Associazione Italiana per la Ricerca sul Cancro (AIRC), con la quale abbiamo co-finanziato, per un importo complessivo di 600 mila euro, due importanti protocolli scientifici, i cui primi risultati saranno prossimamente diffusi anche attraverso apposite iniziative con gli organi di comunicazione e di stampa.

Sono altresì in corso serrati contatti con l'Organizzazione Mondiale della Sanità (OMS), con la quale, per il tramite della Federazione Mondiale del Termalismo e Climatismo (Femtec) stiamo varando un progetto di metanalisi dell'intera letteratura scientifica mondiale in ambito termalístico, primo passo verso lo sviluppo di linee guida accreditate della terapia termale.

La Fondazione ha poi esteso il proprio campo di azione anche oltre oceano: stiamo infatti vagliando la possibilità di una collaborazione scientifica con un'importante università statunitense che ha manifestato interesse ad effettuare uno studio clinico sulla valenza di alcune acque termali in materia di medicina riabilitativa.

Tuttavia, non possiamo ignorare le trasformazioni occorse negli anni più recenti che, aggiunte alle severe economie di bilancio attuate da Regioni ed Enti Locali anche con riferimento alle prestazioni sanitarie, hanno contribuito alle pesanti ricadute sulla domanda di cure termali.

Ed è in questo quadro che si inserisce l'impegno della Fondazione a voler dare massimo rilievo e visibilità ai risultati scientifici sino ad oggi raggiunti, cercando di stimolare l'interesse verso la FoRST, da parte degli organi di comunicazione e di stampa e di accreditarne l'operato presso le più quotate organizzazioni scientifiche e con il mondo della medicina in generale.

A tutto ciò si aggiunge l'importante obiettivo di informare e sensibilizzare il cittadino "utente" anche attraverso iniziative promo/educative, o focalizzate su specifiche patologie, o rivolte a fasce di popolazione con esigenze legate oltreché all'aspetto strettamente sanitario, a quello del raggiungimento del benessere psico-fisico.

A handwritten signature in blue ink, reading "Fulco Primi". The signature is written in a cursive style with a blue ink color.

LA FONDAZIONE

La Fondazione per la Ricerca Scientifica Termale, costituita in ente senza fini di lucro da Federterme, è un'istituzione indipendente specificamente dedicata alla promozione della ricerca nel campo della medicina termale.

Attiva dal 2003, la Fondazione promuove un approccio razionale e moderno di ricerca di base e applicata sulle terapie termali avvalendosi di tutte le tecniche biomediche di indagine.

Dotare la medicina termale di una base scientifica sempre più solida, promuovere lo sviluppo e la condivisione delle conoscenze e garantire alla medicina termale lo status di pratica medica moderna e scientificamente provata sono infatti gli obiettivi della Fondazione, che rappresenta un esempio unico, per settore di competenza e finalità, nel panorama europeo.

Caratterizza l'approccio della Fondazione una visione multidisciplinare che, superando la tradizionale concezione di salute legata all'assenza di patologie, integra i concetti di prevenzione, cura e riabilitazione ed analizza gli effetti biologici, clinici e socio-economici della terapia termale.

Oltre a sostenere economicamente il termalismo scientifico l'attività della Fondazione, finanziata dai fondi provenienti dalle aziende termali, si concretizza nella definizione degli indirizzi di ricerca, con lo scopo di colmare vuoti scientifici attraverso l'approfondita valutazione sullo stato della ricerca termale in ambiti specifici di riferimento.

Con queste premesse risulta evidente come lo scopo della ricerca scientifica termale consista nell'individuazione di nuovi protocolli terapeutici che, affiancati a terapie termali già riconosciute e apprezzate per la loro efficacia nel trattamento di una pluralità di patologie, costituiscono un importante strumento a disposizione della comunità scientifica e offrono una concreta opportunità di riduzione della spesa sanitaria nazionale.

In sintesi, l'alleanza tra termalismo e ricerca scientifica promuove la definizione di una medicina ausiliaria, volta al mantenimento e al recupero della salute, che integra i metodi curativi tradizionali nell'interesse di tutti gli attori coinvolti: pazienti, Sistema Sanitario Nazionale, Inps, Inail e Assicurazioni.

In una prospettiva più ampia, che colloca l'attività termale tra le componenti dominanti dell'economia italiana, l'attività della Fondazione promuove ed esalta il ruolo delle terme moderne: una componente strutturata, organizzata e già fruibile della welfare community.

I PROGETTI E LE RISORSE

Sulla base di un Accordo sottoscritto fra Federterme, il Ministero della Salute e le Regioni, a partire dall'anno 2000 le Aziende termali italiane hanno iniziato ad accantonare lo 0,30% (0,40% nel solo 2004) del fatturato SSN lordo ticket presso un Fondo, appositamente costituito presso Federterme, per la realizzazione di iniziative di ricerca scientifica in campo termale. Nel gennaio 2003, al fine di consentire una più corretta operatività nella gestione dei fondi raccolti, è stata istituita da Federterme, con l'assenso del Ministero della Salute e delle Regioni, la "Fondazione per la Ricerca Scientifica Termale" - FoRST cui è stata riconosciuta personalità giuridica nel settembre 2003.

Dall'anno 2000 e sino al 31.12.2011, la Fondazione ha raccolto circa 5 milioni di euro, impegnando in progetti di ricerca più di 6 milioni di euro.

La Fondazione, amministrata da un CdA misto pubblico-privato, ha lanciato dal 2004 ad oggi ben nove bandi di ricerca, mettendo in moto 73 progetti e cofinanziandone 56, di cui 23 pubblicati su riviste impattate, 7 in corso di pubblicazione e 26 conclusi o in fase di chiusura.

Gli ambiti nosologici di riferimento dei bandi sono i seguenti:

Reumatologia-Ortopedia
Otorinolaringoiatria
Broncopneumologia
Patologie dermatologiche
Patologie dell'apparato digerente e urinario
Sistema cardiovascolare
Terapia della riabilitazione con mezzo termale
Igiene e Microbiologia nelle strutture termali
Farmacoeconomia

A far data dal 1° gennaio 2010, così come previsto dall'Accordo Nazionale per il rinnovo delle tariffe per le prestazioni termali a valere sul biennio 2008-2009, le Aziende Termali versano lo 0,30% di loro spettanza direttamente alla FoRST. Nell'ambito dell'Accordo sopra citato Federterme e le Regioni si sono impegnate a definire, in tempi prefissati, una "scheda sanitaria" sulla base di quella progettata dall'Istituto Superiore di Sanità e realizzata con il contributo economico della Fondazione, con l'obiettivo di procedere alla sistematica rilevazione dei dati clinici e sociali relativi ai soggetti in cura termale e con possibilità di ricavare su basi statisticamente significative elementi epidemiologicamente utili sia ai fini della valutazione degli effetti della terapia termale effettuata, sia ai fini di carattere sanitario generale, in ordine alla prevenzione e alla cura delle malattie, nonché alla riabilitazione.

FORST IN CIFRE

€ 5.000.000
i fondi raccolti
dal 2000 al 2011

€ 6.000.000
il totale dei fondi impegnati
a favore della ricerca

9
i bandi lanciati
dall'inizio dell'attività

73
i progetti di ricerca attivati

56
i progetti di ricerca
cofinanziati

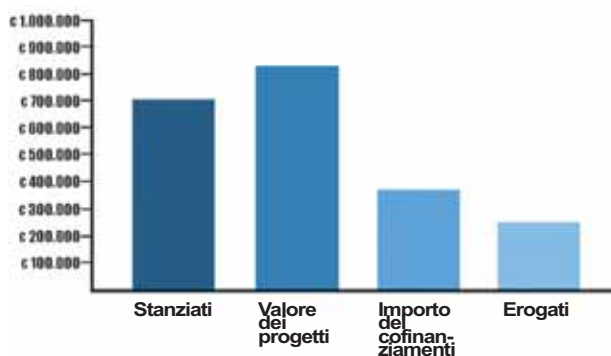
26
i progetti di ricerca
conclusi

23
i progetti di ricerca
pubblicati su riviste
impattate

PROGETTI PUBBLICATI

I BANDO [ANNO 2004]

- Progetti pervenuti: 46
- Progetti cofinanziati: 9
- Stanzianti: € 700.000
- Valore dei progetti: € 810.000
- Importo dei cofinanziamenti: € 385.800
- Erogati: € 249.910,00



Tutti i progetti sono stati conclusi
N. 4 lavori pubblicati - (abstract in calce)
N. 1 revocato

Exogenous Hydrogen Sulfide Induces Functional Inhibition and Cell Death of Cytotoxic Lymphocytes Subsets.

Prisco Mirandola¹, Giuliana Gobbi¹, Ivonne Sponzilli¹, Maurizia Pambianco², Chiara Malinverno³, Antonio Cacchioli³, Giuseppe De Panfilis⁴, and Marco Vitale¹

1 Department of Anatomy, Pharmacology & Forensic Medicine, Human Anatomy Section, University of Parma, Ospedale Maggiore, via Gramsci, Parma, Italy; 2 Terme di Sirmione, Cell Biology Laboratory, Terme di Sirmione, Brescia, Italy; 3 Department of Animal Health, University of Parma, Italy; 4 Department of Surgery, Section of Dermatology, University of Parma, Italy

The toxic effects of exogenous hydrogen sulfide on peripheral blood lymphocytes have been investigated in detail. Hydrogen sulfide is now considered as a gasotransmitter with specific functional roles in different cell types, like neurons and vascular smooth muscle. Here we show that exogenous hydrogen sulfide induces a caspase-independent cell death of peripheral blood lymphocytes that depends on their intracellular glutathione levels, with a physiologically relevant subset specificity for CD8⁺ cells and NK cells. Although lymphocyte activation does not modify their sensitivity to HS⁻, after 24 h exposure to hydrogen sulfide surviving lymphocyte subsets show a dramatically decreased proliferation in response to mitogens and a reduced IL-2 production. Overall, our data demonstrate that HS⁻ reduces the cellular cytotoxic response of peripheral blood lymphocytes as well as their production of IL-2, therefore deactivating the major players of local inflammatory responses, adding new basic knowledge to the clinically well known anti-inflammatory effects of sulfur compounds.

J. Cell. Physiol. 213: 826–833, 2007.
2007 Wiley-Liss, Inc. ORIGINAL ARTICLE 826 Journal of Cellular Physiology

Hydrogen sulfide prevents apoptosis of human PMN via inhibition of p38 and caspase 3.

Laura Rinaldi¹, Giuliana Gobbi¹, Maurizia Pambianco², Cristina Micheloni¹, Prisco Mirandola¹ and Marco Vitale^{1,3}

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Hydrogen sulfide, together with carbon monoxide and nitric oxide, is now considered a gasotransmitter able to induce specific cellular responses. As hydrogen sulfide is a component of several natural compounds known to be effective in many inflammatory pathologies, particularly of the respiratory tract, we studied its effects in vitro on the survival and bactericidal activity of purified human neutrophils. We found that (1) HS⁻ ions promote the survival of granulocytes, but not that of lymphocytes or eosinophils, cultured in serum-free medium; (2) the pro-survival effect of HS⁻ is due to inhibition of caspase-3 cleavage and p38 MAP kinase phosphorylation; (3) the bactericidal activity of neutrophils is not impaired by hydrogen sulfide. We conclude that HS⁻ promotes the short-term survival of neutrophils potentially accelerating the resolution of inflammatory processes and preventing the occurrence of new ones.

Laboratory Investigation (2006) 86, 391-397 © 2006 USCAP, Inc
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www.laboratoryinvestigation.org

Effects of sulfurous, salty, bromic, iodine thermal water nasal irrigations in nonallergic chronic rhinosinusitis: a prospective, randomized, double-blind, clinical, and cytological study.

Ottaviano G, Marioni G, Staffieri C, Giacomelli L, Marchese-Ragona R, Bertolin A, Staffieri A.
Otolaryngology Section, Department of Medical and Surgical Specialties, University of Padova, Padova, Italy.

OBJECTIVES: Nasal irrigations are mentioned among the adjunctive measures for treating several sinonasal conditions. Hyperchromatic supranuclear stria (HSS) in the ciliated cells (CCs) has recently been suggested as a potential cytological marker of the anatomofunctional integrity of nasal mucosa. The aim of this study was to compare the effects of nasal irrigations with sulfurous, salty, bromic, iodine (SSBI) thermal water or isotonic sodium chloride solution (ISCS) in patients with nonallergic chronic rhinosinusitis, considering the endoscopic, functional, microbiological, and cytological evidence (including the ratio of HSS-positive CCs to total CCs [the HSS+ rate]).

METHODS: In a prospective, randomized, double-blind setting, 80 patients were recruited for nasal irrigations with SSBI water or ISCS for 1 month.

RESULTS: An endoscopically assessed significant clinical improvement was seen after both SSBI thermal water and ISCS irrigations. Before treatment, *Staphylococcus aureus* was isolated in 5 patients in the SSBI thermal water group and 4 in the ISCS group. After the nasal irrigations, there was no sign of the bacteria in either group. Only the SSBI water irrigations significantly reduced total nasal resistance, as determined by rhinomanometry. Mild nasal irritation (6 cases) and episodes of extremely limited epistaxis (5 cases) were only reported after SSBI thermal water irrigations. Neither type of nasal irrigation significantly increased the mean HSS+ rate at cytological control after 1 month.

CONCLUSIONS: Both types of nasal irrigation improved the endoscopic and microbiological features of patients with nonallergic chronic rhinosinusitis, whereas only SSBI irrigations significantly reduced total nasal resistance. Further investigations are needed based on longer treatments and follow-up periods to establish whether the HSS+ rate is useful for monitoring clinical improvements in chronic rhinosinusitis treated with nasal irrigations.

Am J Otolaryngol. 2010 May 25. Copyright © 2010. Published by Elsevier Inc.

PMID: 20537762 [PubMed - as supplied by publisher]

Short- and long-term effects of spa therapy in knee osteoarthritis

Fioravanti A, Iacoponi F, Bellisai B, Cantarini L, Galeazzi M.
Rheumatology Unit, Department of Clinical Medicine and Immunological Sciences, University of Siena, Siena, Italy.

OBJECTIVE: To assess both the short- and long-term effectiveness of spa therapy in patients with primary knee osteoarthritis in a prospective, randomized, single-blinded, controlled trial.

DESIGN: Eighty outpatients were enrolled in this study; 40 patients were treated with a combination of daily local mud packs and bicarbonate-sulfate mineral bath water from the spa center of Rapolano Terme (Siena, Italy) for 2 wks, and 40 patients continued regular, routine ambulatory care. Patients were assessed at baseline time; after 2 wks; after 3, 6, and 9 mos after the beginning of the study and were evaluated by Visual Analog Scale for spontaneous pain, Lequesne index, Western Ontario and McMaster Universities Index for gonarthrosis, Arthritis Impact Measurement Scale-1, and symptomatic drug consumption.

RESULTS: We observed a significant improvement of all evaluated parameters at the end of the cycle of spa therapy, which persisted throughout the whole of the follow-up period, whereas in the control group no significant differences were noted. This symptomatic effect was confirmed by the significant reduction of symptomatic drug consumption. Tolerability of spa therapy seemed to be good, with light and transitory side effects.

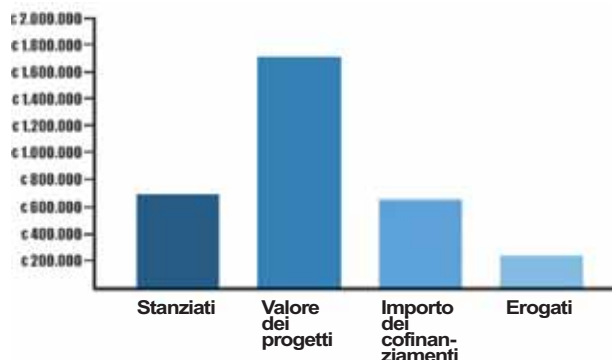
CONCLUSIONS: The results from our study confirm that the beneficial effects of spa therapy in patients with knee osteoarthritis lasts over time, with positive effects on the painful symptomatology and a significant improvement on functional capacities. Spa therapy can represent a useful backup to pharmacologic treatment of knee osteoarthritis or a valid alternative for patients who do not tolerate pharmacologic treatments.

Am J Phys Med Rehabil. 2010 Feb;89(2):125-32.

PROGETTI PUBBLICATI

II BANDO [ANNO 2005]

- Progetti pervenuti: 52
- Progetti cofinanziati: 20
- Stanziati: € 700.000
- Valore dei progetti: € 1.701.225
- Importo dei cofinanziamenti: € 690.950
- Erogati: € 209.848,34



N. 4 lavori pubblicati - (abstract in calce)
N. 7 revocati

Hydrogen sulfide impairs keratinocyte cell growth and adhesion inhibiting mitogen-activated protein kinase signaling.

Giuliana Gobbi^{1,2}, Francesca Ricci¹, Chiara Malinverno¹, Cecilia Carubbi¹, Maurizia Pambianco³, Giuseppe de Panfilis⁴, Marco Vitale^{1,2} and Prisco Mirandola^{1,2}

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The effects of exogenous hydrogen sulfide (H₂S) on normal skin-derived immortalized human keratinocytes have been investigated in detail. We show in vitro that exogenous hydrogen sulfide reduces clonal growth, cell proliferation and cell adhesion of human keratinocytes. H₂S, in fact, decreases the frequency of the putative keratinocyte stem cell subpopulation in culture, consequently affecting clonal growth, and impairs cell proliferation and adhesion of mature cells. As a mechanistic explanation of these effects, we show at the molecular level that (i) H₂S reduces the Raf/MAPK kinase/ERK signaling pathway; (ii) the reduced adhesion of sulfur-treated cells is associated to the downregulation of the expression of b4, a2 and a6 integrins that are necessary to promote cell adhesion as well as anti-apoptotic and proliferative signaling in normal keratinocytes. One specific interest of the effects of sulfurs on keratinocytes derives from the potential applications of the results, as sulfur is able to penetrate the skin and a sulfur-rich balneotherapy has been known for long to be effective in the treatment of psoriasis. Thus, the relevance of our findings to the pathophysiology of psoriasis was tested in vivo by treating psoriatic lesions with sulfurs at a concentration comparable to that most commonly found in sulfurous natural springs. In agreement with the in vitro observations, the immunohistochemical analysis of patient biopsies showed a specific downregulation of ERK activation levels, the key molecular event in the sulfur-induced effects on keratinocytes. KEYWORDS: flow cytometry; western blot; MAPK; skin; NaHS.

Laboratory Investigation (2009), 1-13 © 2009 USCAP, Inc. All Rights Reserved 0023-6837/09 \$32.00

Effects of Inhalation of Thermal Water on Exhaled Breath Condensate in Chronic Obstructive Pulmonary Disease

Gabriella Guarnieri a, Silvia Ferrazzoni a, Maria Cristina Scarpa a, Alberto Lalli b, Piero Maestrelli a
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b Centro Studi Termali Pietro d'Abano, Montegrotto Terme-Abano Terme, Padova, Italy

Key Words Lung function _ Normal saline _ Aerosol therapy _ Leukotriene B 4 _ Pulmonary inflammation

Inhalation of thermal water (TW) is traditionally used as part of the treatment of chronic obstructive pulmonary disease (COPD), but its benefit and mechanisms are controversial. We previously observed a reduced proportion of neutrophils in induced sputum after treatment with TW. The aim of this study was to determine whether inhalation of TW in COPD patients is associated with biochemical changes of airway lining fluid, including a reduction in the neutrophil chemoattractant leukotriene B 4 (LTB 4). Thirteen COPD patients were randomly assigned to receive a 2-week course of TW and normal saline inhalation in a cross-over, single-blind study design. Exhaled breath condensate (EBC) was collected before and after treatments. LTB 4 concentrations in EBC were determined by ELISA, and EBC pH was measured before and after argon deaeration. No significant differences in LTB 4 concentrations in EBC were detected with either treatment. A significant decrease in pH of non-deaerated EBC was observed after a standard course of TW (median 7.45, interquartile range 6.93–7.66, vs. median 6.99, interquartile range 6.57–7.19; p = 0.05), which disappeared after argon deaeration. In conclusion, there is no evidence that TW treatment affects LTB 4 concentration in EBC. The results of EBC pH measurements suggest that TW inhalation induces an imbalance of volatile components of the buffer system in airway lining fluid.

Clinical Investigations Respiration DOI: 10.1159/000227801
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Functional and Histologic Assessment of Rat Gastric Mucosa after Chronic Treatment with Sulphurous Thermal Water

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Key Words

- Sulphurous thermal water
- Gastric acid secretion
- Gastric mucosal defense
- Ethanol
- Indomethacin

The effect of a chronic (4 weeks) administration of sulphurous thermal water on gastric acid secretion and mucosal defense was investigated in rats. Animals were randomized to receive daily intake of tap water or of thermal water obtained from a local spa center (Tabiano, Parma, Italy). Rats were followed for one month as for water and food consumption, body weight and general conditions. At the end of the watering period, the following study protocols were carried out: (a) study of basal and stimulated gastric acid secretion under general anesthesia, and (b) study of the gastric mucosal resistance against the damage induced by ethanol and indomethacin in conscious rats. Basal acid secretion and the acid response to pentagastrin or to histamine were similar in rats assuming ordinary drinking water or thermal water. As for resistance to gastric damage, istological, but not macroscopic, evaluation revealed that rats which assumed thermal water were slightly more resistant to the gastrolesive effect of ethanol (either absolute or diluted). Again, when indomethacin was used as a noxious stimulus, no difference was noted between the two groups as for macroscopic damage; only a nonsignificant reduction of damage was observed histologically in stomachs of rats assuming thermal water. In conclusion, these results indicate that chronic treatment of rats with thermal water, rich in sulphur compounds, may have only minimal effects on the rat gastric mucosa and did not significantly affect mucosal defense mechanisms. The observed tendency to gastroprotection would possibly need further investigation with longer periods of administration.

Pharmacology 2010; 85:146-152 (DOI: 10.1159/000280603)
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Effectiveness of Ischia thermal water nasal aerosol in children with seasonal allergic rhinitis: a randomized and controlled study

M. Miraglia Del Giudice¹, F. Decimo¹, N. Maiello¹, S. Leonardi², G. Parisi³, M. Golluccio², M. Capasso¹, U. Balestrieri¹, A. Rocco¹, L. Perrone¹ and G. Ciprandi⁴

1 Pediatric Department "F.Fede", II University of Naples, Naples; 2 Pediatric Department, University of Catania; 3 UOC Pediatrics and Neonatology, ASL Na-2, PO "Anna Rizzoli", Lacco Ameno; 4 Azienda Ospedaliera Universitaria San Martino, Genova, Italy

Allergic rhinitis is characterized by local inflammation. Nasal lavage may be a useful treatment, however, there are few studies on this topic. This study aims to evaluate the effects of Ischia thermal water nasal irrigation on allergic rhinitis symptoms and airway inflammation during the period of natural exposure to *Parietaria* pollen in children with allergic rhinitis and intermittent asthma. Forty allergic children were randomly divided into two groups: the first group (Group 1) practiced crenotherapy with thermal water aerosol for 15 days per month, for three consecutive months, the control group (Group 2) was treated with 0.9% NaCl (isotonic) solution. In addition, all children were treated with cetirizine (0.5 gtt./kg/day once daily). Nasal symptom assessment, including Total Symptom Score (TSS), spirometry, and exhaled nitric oxide (FeNO) were considered before the treatment (T0), at the end of the treatment (T1) and again 2 weeks after the end of the treatment (T2). The study was registered in the Clinical Trials.gov (NCT01326247). Thermal water significantly reduced both TSS and FeNO levels and there was a significant relationship between reduction of nasal symptoms and FeNO values at the end of treatment with thermal water. In conclusion, this study shows that nasal crenotherapy with the hypermineral chloride-sodium water of Ischia was effective in children with seasonal allergic rhinitis based on the sensitivity to *Parietaria*. These results demonstrate that this natural treatment may be effective in a common and debilitating disease such as the allergic rhinitis.

Keywords: thermal water, nasal lavage, Ischia, allergic rhinitis, children

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ELENCO PROGETTI III B A N D O

PROGETTI BANDO III

Totale importo cofinanziamento € 1.280.000

N° ENTE PRESENTATORE	COORDINATORE	TITOLO PROGETTO
1. DIPARTIMENTO DI MORFOLOGIA ED EMBRIOLOGIA UNIVERSITA' FERRARA	PROF. GIORGIO ZAULI	"Effects of exogenous hydrogen sulfide on endothelial functions and potential interplay with TNF-family members"
2. DIPARTIMENTO DI PNEUMOLOGIA FONDAZIONE MAUGERI	DOTT.SSA SIMONETTA BALDI	"Effects of mud bath therapy in chronic obstructive pulmonary disease"
3. DIPARTIM. DI SCIENZE DELLO SPORT, NUTRIZIONE E SALUTE UNIVERSITA' DI MILANO	PROF. ARSENIO VEICSTEINAS	"Cardiovascular response to SPA treatment (mud and thermal water) in the elderly. Role of baroreflex mechanism"
4. DIPARTIMENTO DI FARMACOLOGIA SPERIMENTALE UNIVERSITA' DI NAPOLI FEDERICO II	PROF. GIUSEPPE CIRINO	"A role for hydrogen sulphide in lung pathophysiology"
5. DIPARTIMENTO DI MEDICINA CLINICA E SPERIM. SEZ.FARMACOLOGIA UNIVERSITA' FERRARA	PROF. PIER ANDREA BOREA	"Hydrogen sulfide and adenosine: a possible role in skin inflammation"
6. DIPARTIMENTO DI PSICHIATRIA, NEUROBIOLOGIA, FARMACOLOGIA E BIOTECNOLOGIA UNIVERSITA' DI PISA	PROF. ANTONIO LUCACCHINI	"Effects of balneotherapy treatment at Montecatini Terme spa on biochemical markers in fibromyalgia patients"
7. DIPARTIMENTO DI SANITA' PUBBLICA E BIOLOGIA CELLULARE- PARASSITOLOGIA UNIV. ROMA TOR VERGATA	PROF. DAVID DI CAVE	"Toward the establishment of a Manual of the Management of Microbiological Safety in Thermal Spa Structures"
8. DIPARTIMENTO DI BIOSCIENZE E BIOTECNOLOGIE UNIVERSITA' DI MODENA E REGGIO EMILIA	PROG. DANIELA GIULIANI	"Spa-waters with high hydrogen sulfide contents against progression of experimental Alzheimer's disease"
9. DIPARTIMENTO DI FISIOPATOLOGIA CLINICA LABORATORIO GASTROENTEROLOGIA UNIVERSITA' DI FIRENZE	PROF. ANDREA GALLI	"Therapeutic effects of thermal water on chronic gastrointestinal diseases!"
10. DIPARTIMENTO DI SCIENZE DELLA SALUTE UNITA' IGIENE E SALUTE PUBBLICA UNIVERSITA' ROMA FORO ITALICO	PROF. VINCENZO ROMANO SPICA	"Development of advanced systems for monitoring/managing hygiene quality and safety in spa structures"
11. LABORATORIO DI IMMUNOLOGIA GENETICA ISTITUTO ORTOPEDICO RIZZOLI	DOTT. FRANCESCO GRASSI	"Role of H2S in the regulation of bone cells"
12. DIPARTIMENTO DI SCIENZE PUBBLICHE UNIVERSITA' DI PARMA	PROF. LORIS BORGHI	"The links between water and salt intake, body weight, hypertension and kidney stone: a difficult puzzle"
13. DIPARTIMENTO DI SCIENZE BIOMEDICHE E BIOTECNOLOGIE UNIVERSITA' DI BRESCIA	PROF. MAURIZIO MEMO	"Effects of sulphurous thermal water on immune response and redox profile"



III BANDO [ANNO 2010]

Progetti pervenuti: 25

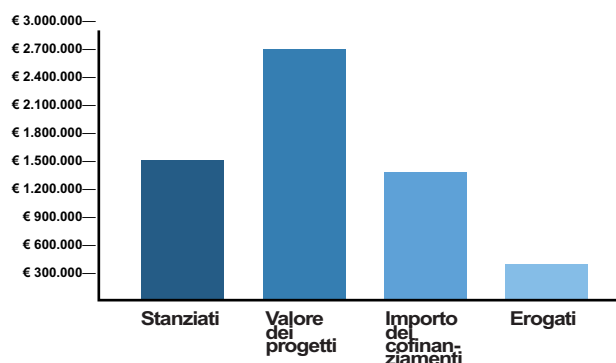
Progetti cofinanziati: 13

Stanziati: € 1.500.000,00

Valore dei progetti: € 2.686.000,00

Importo dei cofinanziamenti: € 1.280.000,00

Erogati: € 385.792,70



N. 2 lavori pubblicati - (abstract in calce)

Hydrogen sulfide down-regulates the expression and release of osteoprotegerin (OPG) by vascular endothelial cells

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Osteoprotegerin (OPG) is a soluble member of the tumor necrosis factor (TNF) receptor family, initially characterized for its ability to inhibit the receptor activator of NfκB ligand (RANKL)-stimulated formation of osteoclasts. OPG also interacts with TNF-related apoptosis inducing ligand (TRAIL), a different member of the TNF super-family whose extracellular domain shares a 35% homology with RANKL. Several studies have demonstrated that OPG is elevated in the serum/plasma of patients affected by different types of cancer, but the potential role of OPG with respect to cancer development/progression is unknown. Among different potential cellular sources of circulating OPG, endothelial cells represent a major source of OPG under basal conditions as well as in response to inflammatory stimuli. Hydrogen sulfide (H₂S)—known for decades as a toxic gas—is endogenously generated from cysteine, in reactions catalyzed by cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE). Mounting data on endogenously generated H₂S have now included this gas in the family of gasotransmitters, together with nitric oxide (NO) and carbon monoxide (CO), and its effects are intensively investigated both at the cellular and molecular level. On these bases, the aim of the present study was to investigate in vitro the effect of H₂S on the expression and release of OPG by human vascular endothelial cells in the absence or presence of the pro-inflammatory cytokine TNF-α.

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Hydrogen Sulfide Is an Endogenous Inhibitor of Phosphodiesterase Activity

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Objective—Recent studies have demonstrated that hydrogen sulfide (H₂S) is produced within the vessel wall from L-cysteine regulating several aspects of vascular homeostasis. H₂S generated from cystathionine γ-lyase (CSE) contributes to vascular tone; however, the molecular mechanisms underlying the vasorelaxing effects of H₂S are still under investigation.

Methods and Results—Using isolated aortic rings, we observed that addition of L-cysteine led to a concentration-dependent relaxation that was prevented by the CSE inhibitors DL-propargylglycine (PAG) and β-cyano-L-alanine (BCA). Moreover, incubation with PAG or BCA resulted in a rightward shift in sodium nitroprusside- and isoproterenol-induced relaxation. Although aortic tissues exposed to PAG or BCA contained lower levels of cGMP, exposure of cells to exogenous H₂S or overexpression of CSE raised cGMP concentration. RNA silencing of CSE expression reduced intracellular cGMP levels confirming a positive role for endogenous H₂S on cGMP accumulation. The ability of H₂S to enhance cGMP levels was greatly reduced by the nonselective phosphodiesterase inhibitor 3-isobutyl-1-methylxanthine. Finally, addition of H₂S to a cell-free system inhibited both cGMP and cAMP breakdown.

Conclusion—These findings provide direct evidence that H₂S act as an endogenous inhibitor of phosphodiesterase activity and reinforce the notion that this gasotransmitter could be therapeutically exploited. **Keywords:** endothelium - hypertension - signal transduction - vascular muscle - vasodilation - cystathionine γ-lyase hydrogen sulfide - cAMP - cGMP - phosphodiesterase.

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BANDI PREMIO 2007 - 2010

A partire dal 2007 FoRST ha bandito annualmente un premio per la ricerca medico-scientifica a favore delle tre migliori pubblicazioni bio-mediche di interesse per il settore termalistico. I lavori scientifici proposti devono essere pubblicati su riviste a diffusione internazionale indicizzate (impact factor), in data non antecedente ai due anni precedenti il bando.

Emanati a partire da febbraio 2008

Stanziati: € 40.000,00

Lavori pervenuti: 19

Lavori premiati: 9

Thermal balneotherapy induces changes of the platelet serotonin transporter in healthy subjects

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Il lavoro mette in evidenza come la sensazione di benessere soggettivo di pazienti sottoposti a trattamento balneotermale ozonizzato sia correlato all'incremento di serotonina, neuro-modulatore implicato in funzioni fisiologiche della psiche. Sono stati studiati 18 soggetti sani, uomini e donne, di età fra 25-50 anni sottoposti a balneoterapia termale ozonizzata a cui si sono misurati prima e dopo il trattamento i parametri ematici piastrinici del Sert. Il trasportatore (Sert) della serotonina (5-HT) è una proteina localizzata a livello dei terminali presinaptici serotoninergici e rappresenta il principale meccanismo che regola la concentrazione sinaptica di 5-HT attraverso un meccanismo attivo di ricaptazione. La nostra ricerca ha verificato modificazioni del SERT, attraverso la valutazione dei parametri (Bmax e Kd) del binding della ³H-paroxetina in membrane piastriniche di 18 soggetti sani prima (t0) e dopo (t1) trattamento balneoterapico in acqua termale. I risultati ottenuti evidenziano un aumento dell'affinità (l'inverso della costante di dissociazione, Kd) del radioligando ³H-paroxetina per il SERT, in tutti i soggetti dopo il trattamento (t1), che si incrementava ulteriormente in quelli dopo una settimana (t2). Queste modificazioni del SERT potrebbero giustificare la sensazione soggettiva di benessere dopo la balneoterapia in acqua termale, rilevata in tutto il campione in esame.

I risultati ottenuti nel nostro studio evidenziano modificazione del SERT (trasportatore della serotonina, neuromediatore maggiormente correlato alla sensazione di benessere soggettivo) successiva ad un trattamento di balneoterapia ozonizzata in acqua termale ipotonica salso-solfato- alcalina di Montecatini, utilizzata per la cura delle vasculopatie periferiche. L'aumento del Sert, indotto dal trattamento termale, sembra responsabile della sensazione di benessere manifestata dai pazienti inseriti nello studio. Lo studio, eseguito in doppio cieco, avvalorava l'importanza dell'ambiente e del mezzo termale nei pazienti sottoposti a crenoterapia aprendo nuovi orizzonti a trattamenti balneoterapici che coinvolgono l'organismo sia nel soma che nella psiche.

Progress in Neuro-Psychopharmacology & Biological Psychiatry 31 (2007) 1436–1439 ELSEVIER

Control of Legionella Pneumophila Contamination in a Respiratory Hydrotherapy System with Sulfurous Spa Water

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Department of Medicine and Public Health, Division of Hy-giene, University of Bologna, Italy (all authors)

Objective: To evaluate the effectiveness of different disinfection treatments in a spa water system contaminated by Legionella pneumophila and associated with a case of Legionella pneumonia.

Design: During an 18-month period, the spa water was analyzed by taking samples from the well, the recirculation line, and the final distribution devices (nebulizers and nasal irrigators). Various attempts were made to eradicate Legionella organisms by chemical and thermal shock. The final protocol consisted of heat shock treatment at 70° C – 75° C for 3 hours, 2 nights per week, followed by a lowering of the water temperature to 30° C ± 1° C for the use in the plant. In addition, 3 times a week superheated steam (at a pressure of 1 atmosphere) was introduced for 1 hour into the nebulization machines.

Setting: A spa at which sulfurous water was used for hydrotherapy by means of aerosol and nasal irrigation.

Patient: A 74-year-old woman with legionnaires disease.

Results. After the case of infection occurred, L. pneumophila was isolated from the recirculation line at a concentration of 400,000 cfu/ L and from the nebulizers and nasal irrigators at levels ranging from 3,300 to 1,800,000 cfu/L. The colonizing organisms consisted of a mixture of L. pneumophila serogroup 1 (12%) and serogroup 5 (88%). The shock treatment with chlorine dioxide and peracetic acid resulted in the eradication of Legionella organisms from the recirculation line but not from the water generated from the final distribution devices. After the restructuring of the plant and the application of thermal shock protocol, an evaluation after 12 months revealed no evidence of Legionella contamination.

Conclusion: To prevent Legionella colonization, disinfection treatment is effective if associated with carefully selected materials, good circuit design, and good maintenance practices

Infection Control and Hospital Epidemiology July 2006, Vol. 27, No. 7

Antioxidant Effect of Sulphurous Thermal Water on Human Neutrophil Bursts: Chemiluminescence Evaluation

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The activities of the HS (sulfhydryl or thiolic) group in the cysteine of glutathione or various low-weight soluble molecules (thiolic drugs), such as N-acetylcysteine, mesna, thiopronine and dithiotreitol or stepronine and erdosteine (prodrugs), include its antioxidant activity in the airways during the release of reactive oxygen or nitrogen species (ROS,RNS) by neutrophils (PMNs) activated in response to exogenous or endogenous stimuli. In addition to being administered by means of thiolic molecules, the HS group can also be given by means of the inhalation of sulphurous thermal water. The aim of this luminol-amplified chemiluminescence (LACL) study was to investigate the effect of sulphurous thermal water on the release of ROS and RNS during the bursts of human PMNs. The water significantly reduced the LACL of fMLP- and PMA-activated PMNs on average from 0.94µg/ml to 15.5µg/ml of HS, even after the addition of L-Arg, a nitric oxide (NO) donor. Similar findings have also been obtained in a cellfree system, thus confirming the importance of the presence of HS group (reductive activity). The positive effects of the activity of sulphurous thermal waters has been partially based on the patients' subjective sense of wellbeing and partially on not always easy to quantify symptomatic (or general) clinical improvements. Our findings indicate that, in addition to their known mucolytic activity and trophic effects on respiratory mucosa, the HS groups present in the sulfurous thermal water of this spring also have antioxidant activity that contributes to the therapeutic effects of the water in upper and lower airway inflammatory diseases.

Key words: Sulphurous thermal water; HS group;Antioxidant activity; PMN; LACL; Cell-free system.

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Possible antioxidant role of SPA therapy with chlorine-sulphur-bicarbonate mineral water

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The aim of our research was to analyze the antioxidant role and efficacy of thermal or salus per aquam (spa) therapy with chlorine-sulphur-bicarbonate mineral water. The study has been performed on 30 rats.

The animals were randomized in three groups, each of them composed by ten animals, denominated A, B and C. The A group was the control group and was not subjected to any specific treatment (placebo); the B group has been treated with a standard cycle of hydroponics treatment with mineral water of Terme di Stabia in Castellammare (Naples, Italy) denominated STABIA; the C group was treated with a standard cycle of hydroponics treatment with mineral water of Terme di Stabia Castellammare (Naples, Italy) denominated SULFUREA.

After two weeks of treatment all the rats were sacrificed and blood was collected for the plasmatic determination of reactive oxygen species (ROS).

The results demonstrated a significant ($P < 0.05$) reduction of ROS in B ($374 \text{ Carr. U} \pm 73$) and C group ($399 \text{ Carr. U} \pm 62$) treated with mineral waters if compared with control group ($571 + 69 \text{ Carr. U}$).

In conclusion this study suggests a possible antioxidant effect of chlorine-sulphur-bicarbonate spa hydroponic treatment with a consequent suitable intestinal physiology, with reduction of the functional and organic modifications that can lead to pathological disorders of the gastroenteric diseases in whole pathogenesis the oxidative stress can develop an important role.

Keyword Spa therapy – Sulphur mineral water – Reactive radicals of the oxygen – Free radicals – Oxidative stress - Polyamines

Amino Acids (2009) 36: 161 – 165 DOI 10.1007/s00726-008-0032-y

Antioxidative effects of sulfurous mineral water: protection against lipid and protein oxidation

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³Terme di Saturnia, Grosseto, Italy

Objectives: To investigate the antioxidative properties of sulfurous drinking water after a standard hydroponic treatment (500 ml day^{-1} for 2 weeks). **Subjects/Methods:** Forty apparently healthy adults, 18 men and 22 women, age 41–55 years old. The antioxidant profile and the oxidative condition were evaluated in healthy subjects supplemented for 2 weeks with (study group) or without (controls) sulfurous mineral water both before (T0) and after (T1) treatment. **Results:** At T1, a significant decrease ($P < 0.05$) in both lipid and protein oxidation products, namely malondialdehyde, carbonyls and AOPP, was found in plasma samples from subjects drinking sulfurous water with respect to controls. Concomitantly, a significant increment ($P < 0.05$) of the total antioxidant capacity of plasma as well as of total plasmatic thiol levels was evidenced. Tocopherols, carotenoids and retinol remained almost unchanged before and after treatment in both groups. **Conclusions:** The improved body redox status in healthy volunteers undergoing a cycle of hydroponic therapy suggests major benefits from sulfurous water consumption in reducing biomolecule oxidation, possibly furnishing valid protection against oxidative damage commonly associated with aging and age-related degenerative diseases.

Keywords: hydroponic treatment; sulfurous mineral water; hydrogen sulfide; thiols; oxidative markers; antioxidant profile

European Journal of Clinical Nutrition (2009) 63, 106–112; doi:10.1038/sj.ejcn.1602892; published online 22 August 2007



The in-vitro percutaneous migration of chemical elements from a thermal mud for healing use

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In-vitro experiments have been developed to ascertain whether pelotherapy applications involve the transfer of chemical elements from the healing mud to the human body, across the skin. All the materials used for therapy (raw clay, mineral water and healing mud obtained after maturation) have been characterised from different points of view (mineralogy, chemistry, exchange properties, radioactivity, grain size and microbiology) in order to get an accurate knowledge of the natural media used for therapy and to follow the development of maturation in the spa centre.

A polymineralic silty clay with rather a common mineralogical and chemical composition is used; the mud is matured in a very saline mineral water, of marine origin, for 5 months. Under these conditions the maturation process increases the dispersion of clay particles and allows cation exchange between clays and water, whereas neither microbiological nor mineralogical changes are detectable. In absence of the biologic indicators of mud maturity, the equilibration of clay with mineral water represents an objective quantitative criterion. In-vitro tests have been carried out by using the Franz-type diffusion cells, which show that the transfer of chemical elements across the skin is very well-developed, and also involving many essential or possibly essential elements. The amounts of chemical elements transferred were compared with toxicological guidelines and with world-wide daily requirement models. No concerns appear from the data, whereas a significant supply of some elements results from a typical application of thermal mud (20 min, full body). The elements which have been considered in order to represent a significant supply are Li, Sr, B, I, Rb, Br, Ba, Na, Cl, Se and Ca, some of these are essential nutrients. The biological effects of the main elements are briefly discussed.

Keywords: Pelotherapy Essential elements Percutaneous absorption

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Has time come for a re-assessment of spa therapy? The NAIADE survey in Italy

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Abstract Goal of this study was to investigate whether appropriately applied spa therapy in several indications could be associated with a subsequent fall in the need for costly health services and missed working days due to sick-leave. The Naiade project was a multicenter observational, longitudinal, questionnaire-based study comparing an "entry" inquiry addressed to patients before an entry thermal cycle, and a "return" inquiry after 1 year. Routine statistical methods were used for comparisons. The study was carried out in 297 of the 340 certified Italian spa centers. Inquiries were managed by the spa doctor(s), with the collaboration of family doctors, and when necessary, hospitals, other health services, labour offices and employers. After exclusion of regular customers and of patients with acute disease phases or severe health conditions, 39,943 patients divided into eight diseases subgroups (rheumatic, respiratory, dermatologic, gynaecologic, otorhynologic, urinary, vascular and gastroenteric) underwent entry inquiry and appropriate spa treatment. Patients who returned for treatment after 1 year ("index year") were 23,680 (59.2%) and received return inquiry. Outcomes considered were: frequency and duration of hospitalisation periods; missed working days; regular use of disease-specific drugs; and resort to "non-spa" rehabilitation therapies. The data collected at return inquiry were compared with those of entry inquiry. All the considered outcomes appeared to be significantly reduced in the index year in seven of the eight disease subgroups in comparison with the previous year. In conclusion, disease-appropriate spa treatments were followed by a reduction in the need of subsequent health interventions in most disease subgroups. The health promoting value of spa treatments should therefore undergo more rigorous assessment with randomised controlled studies.

Keywords Spa treatments* Health resources* Hospital admissions* Sick-leave* Drug consumption

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Effects of Spa therapy on serum leptin and adiponectin levels in patients with knee osteoarthritis

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Abstract Adipocytokine, including leptin and adiponectin, may play an important role in the pathophysiology of osteoarthritis (OA). Spa therapy is one of the most commonly used non-pharmacological approaches for OA, but its mechanisms of action are not completely known. The aim of the present study was to assess whether spa therapy modified plasma levels of leptin and adiponectin in thirty patients with knee OA treated with a cycle of a combination of daily locally applied mud-packs and bicarbonate–sulphate mineral bath water. Leptin and adiponectin plasma levels were assessed at baseline and after 2 weeks, upon completion of the spa treatment period. The concentrations of leptin and adiponectin were measured by ELISA. At basal time, plasma leptin levels were significantly correlated with body mass index (BMI) and gender, but no significant correlation was found with patient age, duration of disease, radiographic severity of knee OA, VAS score or Lequesne index. There was no correlation between plasma adiponectin level and BMI, gender and age, duration of the disease, radiographic severity of knee OA and VAS score. A significant correlation of plasma adiponectin levels was found only with the Lequesne index. At the end of the mud-bath therapy cycle, serum leptin levels showed a slight but not significant increase, while a significant decrease ($P < 0.05$) in serum adiponectin levels was found. However, leptin and adiponectin concentrations after treatment were not correlated with other clinical parameters. In conclusion, our data show that spa therapy can modify plasma levels of the adipocytokines leptin and adiponectin, important mediators of cartilage metabolism. Whether this effect may play a potential role in OA needs further investigations.

Keywords Osteoarthritis _ Leptin _ Adiponectin _ Spa therapy

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The effects of sulfurous-arsenical-ferruginous thermal water nasal irrigation in wound healing after functional endoscopic sinus surgery for chronic rhinosinusitis: a prospective randomized study

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Purpose: Although several publications reported the benefits of nasal irrigation in the management of chronic rhinosinusitis and in sinonasal postoperative care, the available data are poorly controlled.

The aim of this prospective randomized study was to compare the effects of sulfurous-arsenical-ferruginous thermal water nasal irrigation vs isotonic sodium chloride solution nasal irrigation after functional endoscopic sinus surgery (FESS) for chronic sinonasal disease considering the histomorphological characteristics of mucosal repair after sinus surgery.

Materials and Methods: Eighty patients who consecutively underwent FESS were randomly assigned (1:1) to postoperative nasal irrigation with sulfurous-arsenical-ferruginous thermal water or isotonic sodium chloride solution for 6 months. Intraoperative and postoperative (1, 3, and 6 months) mean counts of lymphocytes, neutrophils, eosinophils, plasma cells, histiocytes, and mast cells in ethmoid biopsies were blindly determined by a pathologist.

Results: Fifty-six patients underwent at least 2 postoperative biopsies. A statistically significant reduction of eosinophil count was disclosed 6 months postoperatively only after sulfurous-arsenical-ferruginous solution nasal irrigation ($P = .04$). After isotonic sodium chloride solution nasal irrigation, the mean eosinophil count in 6-month postoperative biopsies did not decrease. After both irrigation modalities, the mean mast cell counts in 6-month postoperative biopsies were significantly lower than in intraoperative biopsies ($P < .05$). Neutrophils, lymphocytes, histiocytes, and plasma cell counts were not significantly different between intraoperative vs 6-month postoperative biopsies independently from irrigation modality.

Conclusions: Considering the important role of eosinophils in allergic response, we should suggest sulfurous-arsenical-ferruginous solution nasal irrigation in particular, which significantly reduces local eosinophil count, for allergic patients after FESS for chronic rhinosinusitis.

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Lavori pervenuti: 8

Lavori premiati: 4

Effects of a low-salt diet on idiopathic hypercalciuria in calcium-oxalate stone formers: a 3-mo randomized controlled trial^{1–3}

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ABSTRACT

Background: A direct relation exists between sodium and calcium excretion, but randomized studies evaluating the sustained effect of a low-salt diet on idiopathic hypercalciuria, one of the main risk factors for calcium-oxalate stone formation, are still lacking.

Objective: Our goal was to evaluate the effect of a low-salt diet on urinary calcium excretion in patients affected by idiopathic calcium nephrolithiasis.

Design: Patients affected by idiopathic calcium stone disease and hypercalciuria (.300 mg Ca/d in men and .250 mg Ca/d in women) were randomly assigned to receive either water therapy alone (control diet) or water therapy and a low-salt diet (low-sodium diet) for 3 mo. Twenty-four-hour urine samples were obtained twice from all patients: one sample at baseline on a free diet and one sample after 3 mo of treatment.

Results: A total of 210 patients were randomly assigned to receive a control diet ($n = 102$) or a low-sodium diet ($n = 108$); 13 patients (2 on the control diet, 11 on the low-sodium diet) withdrew from the trial. At the follow-up visit, patients on the low-sodium diet had lower urinary sodium (mean \pm SD: 86 ± 43 mmol/d at 3 mo compared with 228 ± 57 mmol/d at baseline; $P < 0.001$). Concomitant with this change, they showed lower urinary calcium (271 ± 86 mg/d at 3 mo compared with 361 ± 129 mg/d on the control diet, $P = 0.001$) and lower oxalate excretion (28 ± 8 mg/d at 3 mo compared with 32 ± 10 mg/d on the control diet, $P = 0.001$).

Urinary calcium was within the normal range in 61.9% of the patients on the low-salt diet and in 34.0% of those on the control diet (difference: +27.9%; 95% CI: +14.4%, +41.3%; $P < 0.001$).

Conclusion: A low-salt diet can reduce calcium excretion in hypercalciuric stone formers. This trial was registered at clinicaltrials.gov as NCT01005082

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Biomarkers of oxidation, inflammation and cartilage degradation in osteoarthritis patients undergoing sulfur-based spa therapies

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d Department of Rheumatology, Polytechnic University of Marche, Ancona, Italy

Objectives: To investigate the effects of sulfur-based spa therapies on oxidation, inflammation and cartilage degradation biomarkers in osteoarthritis (OA) patients.

Design and methods: Analyses were performed before therapy (T0), after therapy (T1) and 1 month after its suspension (T2), in OA subjects undergoing mud bath treatments in combination (group A) or not (group B) with hydrotherapy, and compared with those of patients not subjected to spa therapies (group C).

Results: No modifications in plasma/serum biomarker concentrations were observed throughout the study in non-treated patients, while a significant reduction in oxidation, inflammation and cartilage degradation parameters was evidenced in patients of group A. Group B presented a favorable biochemical profile at T1 but not at T2.

Conclusions: To ensure the long term preservation of the chondroprotective effects of sulfur-based therapies, standard mud bath treatments should be associated with hydrotherapy in order to maintain reduced oxidative, inflammatory and degradative stimuli longer.

Keywords: Osteoarthritis, Oxidative stress, Spa therapy, Sulfurous water, Antioxidant protection

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Combination treatment with etanercept and an intensive spa rehabilitation program in active ankylosing spondylitis

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The aim of this study is to determine the effects of a combination treatment with etanercept and spa rehabilitation versus etanercept alone on function, disability and quality of life in a group of patients with active ankylosing spondylitis (AS). Sixty patients with AS underwent etanercept as suggested by ASAS/EULAR recommendations. As the clinical and laboratory conditions improved, 30 patients accepted the proposal of coupling the medical therapy with a 7-day rehabilitation program in a thermal baths centre; the remaining 30 subjects continued to take the biologic agent alone. The comparisons between the 2 groups were made after 3 and 6 months. The primary outcome was an improvement in BASFI. The secondary outcome was an improvement in the visual analogic scale of EuroQol (EQ-5D_{VAS}). After 6 months a statistically significant improvement in BASFI ($p < 0.05$) and EQ-5D_{VAS} ($p < 0.05$) scores was observed in both groups. The mean change in EQ-5D_{VAS} value showed a statistically significant difference in favour of the combination therapy group versus the monotherapy group (22 vs 32, $p < 0.05$). A therapeutic regimen combining etanercept with an intensive rehabilitation program contributes to disability reduction and ameliorates quality of life for AS patients.

Keywords: ankylosing spondylitis, rehabilitation, etanercept, BASFI, quality of life

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Effect of immersion in CO₂-enriched water on free radical release and total antioxidant status in peripheral arterial occlusive disease

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- 5 *Operative Unit of Clinical Pathology, IRCCS Policlinico San Donato, Milan, Italy*

Aim. The aim of this paper was to investigate the release of oxygen free radicals in patients with peripheral occlusive arterial disease and the effects of immersion of the legs and feet in carbon dioxide (CO₂)-enriched water.

Methods. Twenty-five patients with peripheral occlusive arterial disease (Fontaine stage II) and 15 healthy controls were treated by immersing the lower legs in either CO₂ enriched or normal spa water. Blood samples were collected in heparinized tubes and total antioxidant status (TAS) and reactive oxygen metabolites (ROMs) were measured after five treatments a week for two weeks.

Results. d-ROM plasma levels decreased in patients with peripheral occlusive disease after immersion in CO₂-enriched water (P<0.001), and in healthy controls (P<0.01), in line with a significant increase in TAS (P<0.001).

Conclusion. CO₂-enriched water immersion had a positive effect, reducing free radical plasma levels and raising the levels of antioxidants, suggesting an improvement in the microcirculation.

Key words: Free radicals - Reactive oxygen species - Arterial occlusive diseases

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BANDO CONGIUNTO



Per il 2009-2011
AIRC - Associazione Italiana per la Ricerca sul Cancro
e FoRST - Fondazione per la Ricerca Scientifica Termale
hanno emesso un bando congiunto
per uno stanziamento complessivo
di € 600 mila,
di cui:

- € 300 mila AIRC
 - € 300 mila FoRST
- interamente versati

Gli enti aggiudicatari del bando sono:

- Istituto Nazionale dei Tumori di Milano**
Finanziamento € 500 mila (I e II anno)
- Dipartimento di Clinica Medica,
Nefrologia e Scienze della Prevenzione
dell'Università di Parma**
Finanziamento € 100 mila (I e II anno)

Titoli dei progetti:

Istituto Tumori di Milano:
*"Efficacy of thermal treatment for respiratory airways
in heavy smokers"*
Principal Investigator: Dott. Ugo Pastorino

Progetto finalizzato a valutare l'eventuale valenza terapeutica
delle acque termali nel prevenire l'insorgenza
dei fattori di rischio per neoplasie polmonari

Dipartimento di Clinica Medica, Nefrologia
e Scienze della Prevenzione dell'Università di Parma
*"Assessment of lung dose of carcinogens and related
pathobiology in COPD patients inhaling sulphurous water"*
Principal Investigator: Prof. Antonio Mutti

Progetto finalizzato a definire il ruolo dell'inalazione sulfurea
nella correlazione fra COPD e rischio di carcinogenesi
bronco-polmonare

I due progetti, di durata biennale, risultano entrambi in fase conclusiva.

LA RICERCA SCIENTIFICA TERMALE

L'impostazione metodologica della Fondazione per la Ricerca Scientifica Termale (FoRST) è destinata a generare un significativo impulso alla ricerca scientifica di qualità nel settore termalístico.

L'adozione di criteri internazionalmente riconosciuti di giudizio scientifico sui progetti presentati (elenco pubblicazioni, impact factor e altri elementi bibliometrici della produzione scientifica dei proponenti) e la revisione dei progetti esclusivamente da parte di esperti stranieri sono i cardini del recente adeguamento di Fondazione agli standard scientifici internazionalmente riconosciuti per le agenzie di granting della ricerca.

Parallelamente, FoRST ha intrapreso un confronto con realtà termali di altri Paesi europei per stabilire criteri comuni (ad esempio, le parole chiave per rendere omogenei i motori di ricerca sulla materia termale) e si propone un ampliamento su scala non solo europea di questo confronto scientifico tramite organizzazioni internazionali di massimo livello per poter giungere nell'arco dei prossimi 2-3 anni a linee guida condivise sui metodi, indicazioni e trattamenti nell'ambito della medicina termale basati sulle evidenze.

Razionale allocazione dei fondi finalizzata alla ricerca scientifica di qualità ed internazionalizzazione sono le metodologie di FoRST destinate a creare la piattaforma su cui Federterme desidera proseguire il dialogo con le Istituzioni preposte alla tutela della salute, alla prevenzione ed alla formazione sanitaria.

Una analisi più specifica della ricerca che FoRST ha finanziato in questi anni (analisi ovviamente retrospettiva) rivela come la produzione scientifica sia stata comunque di buon livello. In particolare è da segnalare che, in parallelo a studi clinici atti a dimostrare il beneficio tangibile dell'approccio termale in varie patologie, siano finalmente stati implementati con ottimi risultati studi di scienze di base, in cui l'acqua termale è stata sostituita nei saggi in vitro su cellule umane con il principio attivo delle stesse (sali, donatori chimici di sostanze gassose): i risultati sono stati pubblicati su riviste scientifiche di qualità, e la strada per una valutazione scientifica seria basata sulla sperimentazione controllata in vitro è stata tracciata.

Un altro aspetto da sottolineare è il finanziamento che la FoRST ha assegnato, in collaborazione con AIRC all'Istituto Nazionale Tumori di Milano per studiare l'azione termale su una ampia e ben controllata popolazione di fumatori al fine di prevenire almeno in parte gli effetti cronici del fumo sulla mucosa bronchiale. Questo progetto, basato su un rigoroso approccio sperimentale, ha come punto di forza la popolazione dello studio ben controllata e statisticamente assai significativa (diverse migliaia di soggetti) e implica la verifica della valenza preventiva dell'acqua termale sulla precancerosi bronchiale.

Il punto di incontro fra una delle branche della medicina in cui tradizionalmente l'uso delle acque termali ha avuto un suo preciso spazio e queste tematiche di grande valenza riguardo alla prevenzione (con ovvie implicazioni sulla salute pubblica) rappresenta il vero e nuovo punto di partenza della medicina termale moderna.

Prof. Marco Vitale
Coordinatore del Comitato Scientifico FoRST

ESTRATTO DELLO STATUTO DI FoRST

Articolo 2 SCOPI

2.1 La Fondazione prosegue le attività già svolte dal Fondo per la ricerca scientifica termale e si propone lo scopo di promuovere e sostenere l'attività di ricerca medico-scientifica in ambito termale, anche sulla scorta di quanto previsto dalla Legge n. 323/2000.

In particolare si propone di confermare nel tempo, in rapporto all'evoluzione epidemiologica, l'appropriatezza delle cure termali erogate con oneri a carico del SSN, ai sensi dell'art. 4 comma 1 della Legge n. 323/2000.

2.2 Ai fini del comma precedente, la Fondazione, nei limiti e in conformità alle norme di legge applicabili, può promuovere lo svolgimento di convegni, conferenze, programmi di studio e ricerca, intraprendere e promuovere l'attuazione di iniziative di carattere scientifico nel campo della progettazione e promozione della realizzazione delle Opere dell'ingegno, assumere direttamente la gestione di iniziative nel campo della elaborazione di studi progettuali e/o della promozione della realizzazione delle Opere dell'ingegno, sollecitare e sostenere specifici progetti di ricerca di interesse del settore termale, intraprendere qualsiasi altra attività necessaria o utile ai fini del perseguimento dei propri scopi istituzionali.

2.3 Rientrano, altresì, tra gli scopi della Fondazione la stampa e la diffusione, mediante qualsiasi mezzo di comunicazione, anche di massa, ritenuto utile allo scopo, di lavori e pubblicazioni scientifiche in materia termale anche finalizzate alla maggiore conoscenza delle terapie termali e della loro efficacia.

2.4 La Fondazione potrà prestare la propria collaborazione con Enti o Istituzioni, sia pubblici che privati, per il conseguimento degli scopi predetti ed effettuare ogni altra attività necessaria o utile ai fini del perseguimento dei propri scopi istituzionali.

2.5 La presentazione dei progetti di ricerca, finanziabili attraverso il patrimonio della Fondazione, dovrà avvenire da parte dei soggetti indicati e secondo le modalità stabilite dal Regolamento.

2.6 Le finalità della Fondazione sono espletate su tutto il territorio della Comunità Europea.

2.7 Non possono far parte della Fondazione, né possono essere nominati Sostenitori, e se già nominati sono esclusi di diritto, coloro che si trovino in conflitto d'interessi o in situazione d'incompatibilità con la Fondazione. L'esclusione viene dichiarata con deliberazione del Consiglio di Amministrazione.

ESTRATTO DEL REGOLAMENTO DI FoRST

Articolo 6 - SOGGETTI LEGITTIMATI A PRESENTARE E REALIZZARE PROGETTI DI RICERCA

Sono soggetti legittimati a presentare e realizzare progetti di ricerca scientifica finanziabili dalla Fondazione:

- a) Enti di Ricerca nazionali ed internazionali sia pubblici che privati, le Università e le Aziende Sanitarie e Ospedaliere;
- b) gli IRCCS;
- c) le Regioni;
- d) il Ministero della Salute;
- e) l'Istituto Superiore di Sanità;
- f) l'INPS;
- g) l'INAIL.

Articolo 7 - CRITERI DI INAMMISSIBILITA' E DI VALUTAZIONE DEI PROGETTI

O M I S S I S

7.2 La valutazione dei progetti sarà effettuata secondo le seguenti modalità:

Il Comitato Esecutivo della Fondazione per la Ricerca Scientifica Termale è incaricato dell'istruttoria, ed opera una prima analisi dei progetti di ricerca per valutarne l' idoneità formale.

I progetti di ricerca dichiarati ammissibili verranno sottoposti al parere di esperti internazionali di cui al successivo art.10, che dovranno proporre per iscritto un punteggio sulla base dei criteri riportati nel bando.

Il Comitato Esecutivo, acquisiti i pareri del Comitato Scientifico e verificata la congruità del finanziamento richiesto, propone la graduatoria finale alla valutazione del Consiglio di Amministrazione.

7.3 Sulla base dei risultati dell'istruttoria preliminare e della valutazione successiva circa gli aspetti di ordine tecnico-scientifico e finanziario, il Consiglio di Amministrazione della Fondazione per la Ricerca Scientifica Termale approva con propria delibera la graduatoria finale dei progetti, specificando l'entità del finanziamento riconosciuto nonché le modalità e le procedure per l'erogazione dello stesso.

7.4 Le verifiche in itinere ed ex post vengono operate dal Comitato scientifico e dalla Commissione di rendicontazione.

Articolo 8 - MODALITA' DI FINANZIAMENTO

8.1 La Fondazione, secondo le procedure di cui al seguente art. 10, cofinanzierà una quota che in nessun caso potrà eccedere il 60% dell'intero importo previsto per la realizzazione del progetto di ricerca e comunque fino alla concorrenza di un importo massimo di cofinanziamento non superiore ad euro 90.000,00 (novantamila). La percentuale e l'importo massimo di cofinanziamento di cui sopra sono comprensivi dell'eventuale ulteriore contributo per la pubblicazione dei risultati della ricerca su riviste scientifiche con fattore d'impatto citate in ISI/PubMed, il cui ammontare non potrà superare il 30% dell'importo cofinanziato, di cui all'art.12, punto 2.

8.2 Fondazione stipulerà apposita Convenzione con gli Enti beneficiari del cofinanziamento.

Fondazione è abilitata al versamento delle somme oggetto del cofinanziamento unicamente nei confronti dei Soggetti firmatari della Convenzione, i quali sono tenuti all'analitica rendicontazione delle spese sostenute per la realizzazione del progetto di ricerca, secondo i criteri riportati in ciascun bando e allegati alla Convenzione di cui al comma precedente.

8.3 In tutti i casi in cui venga erogato il finanziamento, i lavori scientifici pubblicati ed i relativi risultati rimarranno nella libera disponibilità della Fondazione.

8.4 Nel caso in cui, in riferimento ad un medesimo Bando, vengano ritenuti idonei al finanziamento più progetti, di norma si procederà all'erogazione della quota prevista partendo dal progetto che avrà ottenuto il punteggio più elevato fino a concorrenza dell'importo destinato al singolo Bando.

Articolo 12 - PROCEDURE DI EROGAZIONE DEL CONTRIBUTO

12.1 Il 70% del contributo complessivo che FoRST erogherà all'Ente aggiudicatario sarà versato con le seguenti modalità:

- a. il 20% del contributo, ad avvenuta comunicazione di inizio attività ed in concomitanza alla sottoscrizione della Convenzione;
- b. il 30% del contributo dopo 12 mesi dalla comunicazione di inizio attività e previa presentazione di una relazione scientifica dettagliata dello stato di avanzamento del progetto nonché della rendicontazione contabile delle spese sostenute;
- c. il residuo 20% del contributo alla presentazione dei risultati conclusivi della ricerca (relazione conclusiva) e della rendicontazione analitica delle spese sostenute, secondo i criteri riportati nell'allegato modello di rendicontazione.

12.2 Il 30% della cifra complessivamente riconosciuta verrà infine erogato alla pubblicazione dei risultati della ricerca su riviste scientifiche con fattore d'impatto citate in ISI/PubMed.



I FINANZIATORI

ABRUZZO

- 1 CARAMANICO
- 2 POPOLI

TOT. VERSATO € 97.851,00

BASILICATA

- 1 LUCANE
- 2 RAPOLLA

TOT. VERSATO € 36.981,91

CALABRIA

- 1 ANTONIMINA LOCRI
- 2 CARONTE
- 3 LUIGIANE
- 4 SIBARITE
- 5 SPEZZANO

TOT. VERSATO € 204.937,64

CAMPANIA

- 1 AGNANO
- 2 ANTICHE TERME SAN TEODORO
- 3 ASS.NE ISCHIA
- 4 CAPASSO
- 5 CAPPETTA
- 6 FORLENZA
- 7 PUTEOLANE
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- 9 SCRAJO
- 10 STABIA
- 11 TELESE
- 12 VESUVIANE
- 13 VULPACCHIO

TOT. VERSATO € 731.975,23

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- 1 CASTEL SAN PIETRO DELL'EMILIA
- 2 CERVAREZZA
- 3 FRATTA
- 4 ISTITUTO E. BAISTROCCHI
- 5 CASTROCARO
- 6 CERVIA E BRISIGHELLA
- 7 EUROTERME
- 8 FELSINEE
- 9 MONTICELLI
- 10 PORRETTA
- 11 PUNTA MARINA
- 12 RIMINITERME
- 13 RICCIONE
- 14 RIOLO
- 15 ROSEO
- 16 SANT'ANDREA
- 17 SALSOMAGGIORE
- 18 SALVAROLA
- 19 SANT'AGNESE
- 20 TABIANO

TOT. VERSATO € 1.269.619,11

LAZIO

- 1 ACQUE ALBULE
- 2 ALBA
- 3 ALBERGO CIORRA
- 4 CARACCIOLIO
- 5 COTILIA
- 6 NUOVA SUIO Srl

- 7 POMPEO
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- 9 SANT'EGIDIO
- 10 TOMASSI DI SUIO
- 11 VESCINE
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TOT. VERSATO € 311.656,09

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- 2 FONS SALUTIS
- 3 LURISIA
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TOT. VERSATO € 134.097,62

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- 1 AURORA
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TOT. VERSATO € 44.314,50

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- 3 GERMANI MARINO
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- 5 GRANATA CASSIBILE
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- 14 SATURNIA
- 15 SANT'ELENA
- 16 VENTURINA
- 17 SALUTE AMBIENTE (BAGNI DI PETRIOLO)

TOT. VERSATO € 385.915,87

TRENTINO

- 1 MERANO
- 2 COMANO
- 3 LEVICO

TOT. VERSATO € 104.781,07

UMBRIA

- 1 FONTECCHIO
- 2 SANGEMINI

TOT. VERSATO € 34.754,33

VALLE D'AOSTA

- 1 TERME DI SAINT VINCENT

TOT. VERSATO € 5.129,54

VENETO

- 1 ASS.NE ABANO
- 2 BIBIONE
- 3 HOTEL DOLOMITI
- 4 HOTEL SMERALDO
- 5 HOTEL TERME ASTORIA
- 6 HOTEL TERME BELLAVISTA
- 7 HOTEL TERME BELVEDERE
- 8 HOTEL TERME DELLE NAZIONI
- 9 HOTEL TERME DELTA
- 10 HOTEL TERME ELISEO
- 11 HOTEL TERME EUCALIPTI
- 12 HOTEL TERME INTERNAZIONALE
- 13 HOTEL TERME MARCONI
- 14 HOTEL TERME PRINCIPE
- 15 HOTEL TERME REVELAND
- 16 HOTEL TERME VERDI
- 17 MIRAMONTI
- 18 PARK HOTEL EMILIO VETTORE
- 19 RECOARO
- 20 SALZANO

TOT. VERSATO € 667.130,63

**Totale complessivo regionale
5.059.112,05**

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