MICRA

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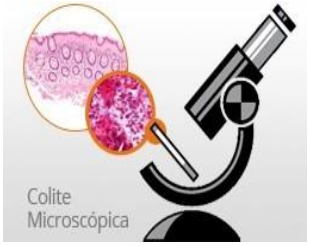
GRUPO DE ESTUDO
DA DOENÇA INFLAMATÓRIA INTESTINAL



An epidemiological study to determine the prevalence of **Mi**croscopic **C**olitis and describe its clinical and histological features among patients with symptoms of ch**R**onic watery diarrhea submitted to colonoscopy **A**ttending to the Portuguese gastroenterology setting **- MICRA**

Study sponsor: Grupo de Estudo da Doença Inflamatória Intestinal (GEDII)

Name of Scientific Coordinator: Prof. Fernando Magro

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Primary Objective

- To determine the prevalence of MC among patients who attend to the specialist appointment with symptoms of chronic, watery diarrhea of unknown etiology for more than 4 week and undergo colonoscopy

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Secondary Objectives

- To determine the prevalence of MC subtypes (collagenous colitis, lymphocytic colitis and incomplete colitis).
- To compare the socio-demographic, clinical and histological characteristics and previous therapies of patients with confirmed diagnosis of MC (MC patients) versus patients without diagnosis of MC (non-MC patients).
- To describe the therapeutic attitude regarding MC patients over a period of 24 months.
- To describe the clinical activity of MC patients over a period of 24 months.
- To describe the histological features of MC patients 24 months after diagnosis.

Secondary Objectives (cont.)

- To explore the association of socio-demographic, clinical and histological characteristics with clinical activity among MC patients followed for 24 months.
- To explore the association of socio-demographic, clinical characteristics with histological activity among MC patients followed for 24 months.
- To explore the correlation of treatments used by MC patients with clinical activity.
- To explore the correlation of treatments used by MC patients with histological activity.
- To explore the correlation between fecal calprotectin, EPC and EPX levels with clinical activity among MC patients

Inclusion Criteria

1. Patients who signed the informed consent

2. Male or female patients, 18 years or older

3. Patients with chronic or intermittent, watery diarrhea of unknown etiology for more than 4 weeks

4. Patients who are eligible for complete colonoscopy according to physician's clinical criteria

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Exclusion Criteria

1. Patients with history of IBDs or any other known intestinal disease
2. Any condition that precludes the patient to undergo complete colonoscopy
3. Patients who are being treated with any investigational agent
4. Pregnancy
5. Patients who are not willing to comply with routine clinical appointments or procedures

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Primary Endpoint

- Number of patients with confirmed diagnosis of MC (any subtype) over the total number of colonoscopies performed in all patients included in the study

Primary Endpoints (cont.)

- Proportion of patients with confirmed diagnosis of each subtype of MC (CC, LC and IC).

- Age, gender, BMI, smoking status, duration of symptoms, stool frequency and consistency (type), familial history of IBDs, comorbidities, previous pharmacological/ non-pharmacological therapies and laboratory parameters will to be compared between MC patients and non-MC patients.

- Treatments (pharmacological/non-pharmacological) prescribed by specialist for patients with MC diagnosis.

- Number of stools and type (Bristol stool form scale), urgency and abdominal pain over the last 7 days before each time point of assessment for patients with MC diagnosis.

- Proportion of MC patients with clinical remission at each data collection time point (month 3, 6, 9, 12, 15, 18, 21 and 24)
  Clinical remission: mean of < 3 stools per day and mean of < 1 watery stool per day

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Secondary Endpoints

- Proportion of MC patients with histological remission at month 24.
  See section 8.3.2 for definition of histological remission

- Age, gender, BMI, smoking status, duration of symptoms, stool frequency and consistency, familial history of IBDs, age at diagnosis of MC, time to diagnosis of MC, comorbidities, pharmacological/non-pharmacological therapies, laboratory parameters and histological features, compared with clinical activity status (active/non active) described for patients with MC diagnosis.

- Age, gender, BMI, smoking status, duration of symptoms, stool frequency and consistency, familial history of IBDs, age at diagnosis of MC, time to diagnosis of MC, comorbidities, pharmacological/non-pharmacological therapies, laboratory parameters, compared with histological features, described for patients with MC diagnosis.

- Area under the ROC curve of fecal calprotectin, ECP and EPX levels with clinical activity at each data collection time points among MC patients.

- Area under the ROC curve of fecal calprotectin ECP and EPX levels with histological activity at each data collection time points among MC patients.

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Study Flowchart

At risk population

Subjects with chronic, watery diarrhea attending to gastroenterologist

Eligibility criteria

Eligible population

Complete colonoscopy

Abnormal

Endoscopic findings indicative of bowel disorders (other than MC)

Normal

Population with histology

Collection of colonic specimens

- Histological findings suggestive of other disorders (other than MC)
- No findings

Population diagnosed with MC

Histological findings confirming Microscopic Colitis

Prospective component (24 months)

- Clinical and histological progression
- Explore prognosis factors

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CHRONOGRAM

	All	24-month prospective part Only for patients with diagnosis of microscopic colitis							
Variables	**BSL**	**M3**	**M6**	**M9**	**M12**	**M15**	**M18**	**M21**	**M24**
Date of birth	X								
Sex	X								
Height	X								
Weight	X	X	X	X	X	X	X	X	X
Smoking status	X								
Medical history	X								
Comorbidities	X								
Symptoms of diarrhea	X	X	X	X	X	X	X	X	X
Prior therapies	X								
Colonoscopy	X								X
Colonic specimen collection	X								X
Histology	X								X
Therapeutic attitude regarding MC (pharmacological/non pharmacological)		X	X	X	X	X	X	X	X
Laboratory parameters[2]	X	X	X	X	X	X	X	X	X
Fecal sample (calprotectin, ECP and EPX levels)	X	X	X	X	X	X	X	X	X
Dispensing of patient diary	X[1]	X	X	X	X	X	X	X	

BSL = baseline: date of the study's first appointment; M= month; ECP= eosinophil cationic protein; EPX= eosinophil protein X

[1] The patient diary will be delivered as soon as the MC diagnosis is confirmed. The diary will be returned by the patient at each appointment and a new diary will be dispensed.

[2] hemoglobin, platelets, leukocytes, neutrophils, eosinophiles, basophiles, monocytes, lymphocytes, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), iron and transferrin.

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Protocolo prático de colheita de amostras

Protocolo de recolha de amostras para doseamento de Calprotectina fecal

(Basal + todas as visitas e VISITA de descontinuação, caso exista)

a) Recolha de fezes

Colher, no mínimo, 2 g de amostra fecal com ajuda do EasySampler kit

Levante o assento da sanita e limpe a superfície

Remova a tira que protege a fita adesiva do EasySampler

Cole metade do EasySampler à parte detrás da sanita. Assegure-se que o centro do EasySampler está formar uma espécie de taça e cole a outra metade do EasySampler à parte frontal da sanita

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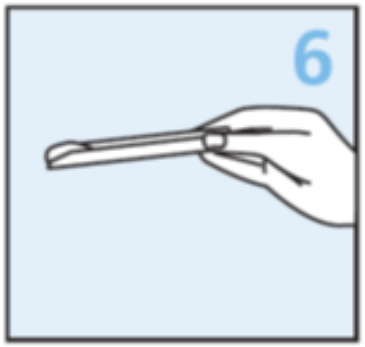
Protocolo prático de colheita de amostras

Baixe o assento da sanita

Defeque



Colha a amostra de fezes

Levante o assento da sanita, descole o EasySampler e puxe o autoclismo, deixando o EasySampler seguir com o fluxo de água

Importante:

Repita a descarga até um fluxo de 10-15 L de água;

Restos de fita adesiva poderão ser removidos com álcool etílico.

b) Armazenamento de amostras de fezes

Para cada doente, a amostra fecal deve ser recolhida, num tubo devidamente identificado*. Será necessário no mínimo 2 g de amostra. As amostras podem ficar armazenadas até ao seu envio, entre 2 a 8ºC, num prazo **máximo de 48 horas após a colheita**.

_____

*** Etiquetas** - no criotubo deverá constar uma etiqueta com a seguinte informação: ***Número do site (centro) + código do doente (CRF) + nº da visita + data de colheita. As etiquetas serão enviadas juntamente com os kits de colheita.***

O centro deverá contactar o GEDII (Dr.ª Sandra Dias, email: gedi@med.up.pt), informando a necessidade do serviço de transporte.

Protocol-Specific Analysis Requisition Form

Study: MICRA

"An epidemiological study to determine the prevalence of Microscopic Colitis and describe its clinical and histological features among patients with symptoms of chRonic watery diarrhea submitted to colonoscopy Attending to the Portuguese gastroenterology setting - MICRA"

Sponsor: GEDII

Site Nr: __ __ __

Patient ID (CRF Nr) #: __ __ __

Week Nr __ __

Date of Birth (month/year): __ __ / __ __ __ __

Gender at birth: ____

Shipped Samples (tick when applicable)	Description	Collection Date (day/month/year)	Sample ID
	Fecal Calprotectin		
	Histology		

REQUESTER INFORMATION

Name: _____ Date: _____

Signature: _____

ENCLOSE THE ORIGINAL OF THIS FORM WITH THE SAMPLES BEING SHIPPED TO THE CENTRAL LAB. A COPY SHOULD BE LEFT AT SITE.

FOR SAMPLE SHIPMENT PLEASE CONTACT GEDII: gedi@med.up.pt