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Effect of L-alanyl L-glutamine dipeptide on diarrhea, treatment response, and patients' survival in colon cancer patients receiving chemotherapy

Submission date
03/03/2022

Recruitment status
No longer recruiting

Registration date
04/03/2022

Overall study status
Completed

Last Edited
08/04/2024

Condition category
Signs and Symptoms

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diarrhea caused by chemotherapy (chemotherapy-induced diarrhea) may represent a life-threatening side effect in cancer patients receiving chemotherapy. FOLFOX, an effective treatment for colon cancer, has been associated with diarrhea with high severity. Management of diarrhea is crucial to increase the survival of cancer patients and to improve the quality of life. Glutamine is an abundant protein-peptide found in blood and may improve diarrhea symptoms. This study aimed to provide evidence that L-alanyl L-glutamine dipeptide may have a positive influence on the incidence of diarrhea, treatment response, and the overall survival in colon cancer patients treated with modified FOLFOX-6 (mFOLFOX-6).

Who can participate?
Patients of both genders, aged ≥18 years with histologically confirmed colon adenocarcinoma; stages II, and III can participate in this study.

What does the study involve?
Patients who are treated with the standard mFOLFOX-6 therapy will be randomly allocated to receive glutamine dipeptide or not receive glutamine dipeptide.

What are the possible benefits and risks of participating?
The expected benefits include a decrease in the incidence of diarrhea together with improvement of the treatment response and the patients' survival compared to the placebo. There are no known risks of participation in this study.

Where is the study run from?
Tanta University (Egypt)

When is the study starting and how long is it expected to run for?
March 2019 to April 2023

Who is funding the study?
Taif University (Saudi Arabia)

Who is the main contact?
Dr Ahmed M. Kabel, ahmed.kabal@med.tanta.edu.eg

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
34918/3

Study information

Scientific Title
The ameliorative potential of L-alanyl L-glutamine dipeptide in colon cancer patients receiving modified FOLFOX-6 regarding the incidence of diarrhea, the treatment response, and patients' survival: a randomized controlled trial

Study objectives

Administration of L-alanyl L-glutamine dipeptide to colon cancer patients receiving modified FOLFOX-6 therapy can efficiently decrease the Incidence of diarrhea and improve the response to treatment and the patients' survival

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/03/2019, Research Ethics Committee of Faculty of Medicine (Tanta University, El-Geish street, Tanta, Egypt, 31527; +201102344533; researchethicscommitteefomtu@gmail.com), ref: 34918/3

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Incidence of diarrhea in colon cancer patients receiving mFOLFOX-6 therapy

Interventions
Treatment Plan (Chemotherapy)
All patients will be treated with the standard mFOLFOX-6 consisting of 2-hour intravenous (IV) infusion of oxaliplatin (85 mg/m²) on day 1, and 2-hour IV drip infusion of calcium folinate (400 mg/m²) on day 1, followed by IV injection of 5-FU (400 mg/m²) and continuous infusion of 5-FU (1200 mg/m²) on days 1-2 (Total 2400 mg/m² over 46-48 hours). The intravenous infusion will be continued every 2 weeks.
Patients will be randomized to receive glutamine dipeptide or not receive glutamine dipeptide (control group). In the glutamine dipeptide group, (N(2)-L-Alanyl-L-Glutamine Dipeptide, (Dipeptiven), by Fresenius Laboratories, Germany) will be given IV in a dose of 20 gm/100ml on the day 1-2 regimen every 2 weeks.

Follow up
The included patients enrolled in both groups will be evaluated at the baseline (prior to chemotherapy) and after two, four, and six cycles of treatment. Treatment response to chemotherapy will be assessed every two cycles according to the Response Evaluation Criteria in Solid Tumors (RECIST). Treatment-related toxicities will be estimated according to standard World Health Organization (WHO) criteria. Diarrhea will be graded according to the National cancer institute. In case of diarrhea grades I and II, only supportive therapy will be considered. Grade III diarrhea will be managed with supportive therapy, IV fluids and hospitalization. Chemotherapy will be postponed till complete recovery and the dose of chemotherapy will be reduced. Regarding patients with grade IV diarrhea, they will be admitted to the ICU and given IV fluids, supportive care, monitoring of electrolytes and chemotherapy will be stopped until complete recovery with dose reduction in case of reinfusion.

The randomization process will be carried out by flipping a coin. One side of the coin will denote the glutamate group and the other side will denote the placebo group.

Intervention Type
Supplement

Primary outcome(s)
At baseline (prior to chemotherapy) and after two, four, and six cycles of treatment:
1. Treatment response to chemotherapy will be assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST)
2. Diarrhea will be graded according to the National cancer institute.

Key secondary outcome(s))
Treatment-related toxicities will be estimated according to standard World Health Organization (WHO) criteria at the baseline and after two, four, and six cycles of treatment

Completion date
01/04/2023

Eligibility

Key inclusion criteria
1. Patients of both genders
2. Aged ≥18 years
3. Have histologically confirmed colon adenocarcinoma stage II, and III according to American Joint Committee on Cancer and the Union for International Cancer Control (AJCC-UICC); 7th Edition
4. Have adequate hematological parameters (evidenced by white blood cell count ≥ 4000/µl and platelet count ≥ 100,000/µl).
5. Have adequate renal (creatinine < 1.5 mg/dl) and hepatic functions (serum total bilirubin < 1.5 mg/dl).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
44

Key exclusion criteria
1. Patients with stage IV colon cancer.
2. Patients with second primary colon cancer.
3. Patients with colon cancer with any other co-morbidity.

Date of first enrolment
01/04/2022

Date of final enrolment
01/08/2022

Locations

Countries of recruitment
Egypt

Study participating centre
Tanta University
El-Geish street
Faculty of Medicine
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Sponsor information

Organisation
Taif University

ROR
https://ror.org/014g1a453

Funder(s)

Funder type
University/education

Funder Name
Taif University

Alternative Name(s)

TU

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Saudi Arabia

Results and Publications

Individual participant data (IPD) sharing plan
Data used and/or analyzed during this study will not be available for public access because of patients' privacy but will be available from the corresponding author upon reasonable request (ahmed.kabal@med.tanta.edu.eg)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/03/2022	08/04/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes