

## **STUDY PROTOCOL**

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### **The Role of Probiotics in Improving Quality of Life in Women with Functional Constipation: Randomized Double-blind Controlled Trial**

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## **I. Introduction**

Functional constipation has a negative impact on patients' quality of life, including in the urban community. Reduction of quality of life consists of social aspect such as psychological disorders, lethargy, anxiety, and also economical aspect such as decreased productivity. One of functional constipation pathophysiology is the intestinal-brain communication disorder (Gut Brain Axis) influenced by hormonal, serotonin production gene variations so as to give a large psychological impact on the sufferer. The negative impact of functional constipation which occurs in 2.5-19% of the world population is especially greater in women. While probiotics have previously been linked with positive results on various gastrointestinal disorders, there has never been a study investigating probiotics positive impact on quality of life in urban women with functional constipation. Thus, this study aims to investigate probiotics effect in improving quality of life in urban women with functional constipation.

## **II. Study Objective**

To investigate the relationship between administration of probiotics and improvement in quality of life in women with functional constipation.

## **III. Study Design**

- Parallel group design, randomized, probiotic versus placebo for 21 days.
- Block randomization using permutation blocks of size 8.
- Double-blinded evaluation.

## **IV. Methodology**

### **Patients**

#### Inclusion Criteria

- Females aged 18 to 60 years
- Being declared healthy based on initial examination and the Structured Interview Questionnaire (SIQ)
- Having the symptoms and signs of functional constipation refer to ROME-IV criteria
- Able to communicate well
- Able to consume 1 bottle of fermented milk each day for three weeks
- Not using antibiotic no later than one week before supplementation

#### Exclusion Criteria

- Diagnosed with functional bowel disorder
- Using anesthesia at least 4 weeks before treatment
- Having a serious pathological disorder (carcinoma)
- During healing phase of acute gastrointestinal disorders at least 4 weeks before treatment
- Having severe heart disease
- Taking chronic medications such as antidepressants or analgesics

## **Study Intervention**

### Drug Presentation

- Test drug: fermented milk containing probiotic *Lactobacillus plantarum* IS-10506.
- Comparator: fermented milk containing placebo.

### Drug Administration

- Each subject receives 1 bottle of fermented milk, to be consumed once daily at the same hour for a duration of 21 days.
- Fermented milk will be stored in a freezer (-16°C) into frozen condition, and must be left at room temperature for several hours before drunk in cold-liquid condition.

### Drug Supply

- Fermented milk containing probiotic and placebo will be supplied by PT Ultra Jaya.

## **Concomitant Medication**

None

## **Primary Endpoint (by blinded evaluator)**

Improvement in quality of life, assessed with PAC-QOL© (Patient Assessment of Constipation – Quality of Life) questionnaire.

## **Sample Size**

The minimum sample size is 62, plus a 10% dropout prediction: 70.

## **Procedure**

All patients will be collected from Puskesmas Petamburan Jakarta.

After signing the informed consent, the subjects will be assessed for eligibility using inclusion and exclusion criteria by medical staff of Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia – Cipto Mangunkusumo Hospital in collaboration with Puskesmas Petamburan Jakarta. The remaining subjects will be randomly allocated into two groups: probiotic group and placebo group, and will be assessed on their initial quality of life with PAC-QOL© (Patient Assessment of Constipation – Quality of Life) questionnaire by trained personnel.

Each subject will receive 1 bottle of fermented milk containing either probiotic or placebo to be consumed once daily at the same hour for a duration of 21 days.

After 3 weeks, the subjects will return to the study site and will be reassessed on their final quality of life with PAC-QOL© (Patient Assessment of Constipation – Quality of Life) questionnaire by trained personnel.

## **V. Data Management and Statistical Analysis**

### **Efficacy Analysis**

Statistical analysis between probiotic versus placebo at 21 days after intervention:

- PAC-QOL© score: use paired T test

## **VI. Ethical Committee Approval**

Approval from the Ethics Committee of the Faculty of Medicine, Universitas Indonesia must be obtained before starting the trial.

## **VII. References**

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