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Molecular basis of depression disorder and influence of omega-3 fatty acid on clinical symptoms and biomarkers

Submission date
10/10/2016

Recruitment status
No longer recruiting

Registration date
19/10/2016

Overall study status
Completed

Last Edited
28/02/2024

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Mood disorders in children and adolescents are a serious problem worldwide and are becoming more common in younger children. In recent years, research has been focused on the adjuvant therapy of depression (extra treatment to enhance the effects of the main treatment) to reduce the consumption of antidepressants, prolong remission (disease-free periods) and improve the outlook for these patients. The use of Omega-3 fatty acids as an adjuvant therapy is promising, with beneficial effects in the prevention and treatment of depression. This study aims to assess the effectiveness of omega-3 fatty acids-rich fish oil in the treatment of depression symptoms in children and adolescents treated for depression as well as to find out what effects this has on the body by looking at biochemical markers (substances).

Who can participate?
Children and adolescents aged 10 -18 years suffering from depression who are registered at the Department of Child Psychiatry of Comenius University and Child University Hospital in Bratislava.

What does the study involve?
Patients are randomly allocated to one of two groups. Those in the first group take 20 mL of omega-3 fish oil emulsion every day for 12 weeks in addition to their usual treatment, followed by 4 weeks of not taking the oil. Those in the second group take 20 mL of omega-6 sunflower oil emulsion every day for 12 weeks in addition to their usual treatment, followed by 4 weeks of not taking the oil. At the start of the study, every two weeks during the 12-week treatment period, and then at 16 weeks, participant have their symptoms of depression assessed and have blood and saliva samples taken to measure for chemical indicators of the effects the supplements are having on the body.

What are the possible benefits and risks of participating?
Participants who receive the omega-3 oil may benefit from a reduction of their depressive symptoms. There are no known risks involved with participating.

Where is the study run from?
1. Comenius University (Slovakia)
2. Comenius University and Child University Hospital (Slovakia)

Who is funding the study?
Slovak Research and Development Agency (Slovakia)

When is the study starting and how long is it expected to run for?
March 2013 to June 2020

Who is the main contact?
Professor Zdenka Durackova
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
APVV-15-0063

Study information

Scientific Title

Molecular bases of depressive disorders in children and adolescents, effect of omega-3 fatty acids, inflammation and oxidative stress

Acronym
Depoxin

Study objectives
Current study hypothesis as of 05/12/2023:
The current study aims to compare the efficacy of 12 weeks of administration of omega-3 fatty acids present in fish oil emulsion with a control oil emulsion (omega-6 fatty acids rich sunflower oil emulsion) alongside standard antidepressant treatment on depressive symptoms in children and adolescents (10 to 18 years old).

The study will investigate:
1. Clinical parameters: CDI score
2. Biochemical parameters: Lipid profile, fatty acid composition in serum LDL- and HDL-subfractions of lipoproteins, markers of oxidative stress and inflammation in blood, steroidal hormones in saliva, metabolites of kynurenine and serotonin pathway
3. Biophysical parameters: Fluidity of erythrocyte membranes
4. The length of telomeres in the buccal cells

Previous study hypothesis:
The aim of the current study is to compare the efficacy of 12 weeks administration of omega-3 fatty acids present in fish oil emulsion with a control oil emulsion (omega-6 fatty acids rich sunflower oil emulsion) alongside standard antidepressant treatment on depressive symptoms in children and adolescents (8 to 18 years old).

The study will investigate:
1. Clinical parameters: CDI score
2. Biochemical parameters: Lipid profile, fatty acid composition in serum LDL- and HDL-subfractions of lipoproteins, markers of oxidative stress and inflammation in blood, steroidal hormones in saliva
3. Biophysical parameters: Fluidity of erythrocyte membranes
4. The length of telomeres in the buccal cells

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/03/2013, Ethics Committee of the National Institute of Children’s Diseases and the Faculty of Medicine, Comenius University Bratislava (Limbova 1, Bratislava, 833 40, Slovakia; +421 2 59371209, +421 2 59371927; detska.klinika@nudch.eu), ref: None available

Study design
Single-centre randomized double-blind comparator controlled interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet in Slovakian

Health condition(s) or problem(s) studied
Depressive disorder (F32) or mixed anxiety and depressive disorder (F41.2)

Interventions
Patients are allocated in a 1:1 ratio to the two arms (Om3 and Om6) according to a computer-generated random sequence using block randomisation with a block-size of four. The randomisation was performed by the independent statistician. Patients are enrolled and assigned sequentially to adjuvant interventions by the physician. The allocation sequence is not available to any member of the research team until the databases had been completed and locked.

Intervention group: Participants receive 20ml of an omega-3 FA rich fish oil emulsion (Om3), which provides 2400 mg of total omega-3 FA; 1000 mg EPA and 750 mg DHA, EPA:DHA ratio = 1.33:1, for 12 weeks in addition to their standard antidepressant therapy, followed by a 4 week wash out period.

Control group: Participants receive an identically looking comparator omega-6 sunflower oil emulsion containing min 2467 mg of omega-6 linoleic acid provided by Cultech Ltd, Port Talbot (UK) for 12 weeks in addition to their standard antidepressant therapy, followed by a 4 week wash out period.

Clinical examinations take place at the beginning of the project (week 0), and every 2 weeks for 3 months (weeks 2, 4, 6, 8, 10, 12) and after following 4 week wash-out period, at week 16. Ratings aree made using the self rated scale Children's Depression Inventory (CDI). Biological samples (blood, urine, saliva) are taken at the week 0, 6, 12 and 16.

Intervention Type
Supplement

Primary outcome measure
Clinical symptoms of depression are determined using Children's Depression Inventory score (CDI) at baseline, 2, 4, 6, 8, 10, 12 and 16 weeks.

Secondary outcome measures
1. Basic biochemical marker levels (glucose, uric acid, lipid profile (total cholesterol, LDL-CH, HDL-CH, TAG), creatinine, CRP, liver enzymes ALT, AST) are measured by testing blood samples taken at baseline, at the week 6 and 12 of intervention and after wash-out period, at the week 16
2. Markers of oxidative stress (antioxidant enzymes SOD, GPx, CAT in Er, PON1 in serum, markers of lipid damage - lipoperoxides, 8-IsoP, protein damage - AOPP, serum protein carbonyls, nitrotyrosine, DNA damage in lymphocytes by comet assay, total antioxidant status-TEAC) are measured by testing blood samples taken at baseline, at the week 6 and 12 of intervention and

after wash-out period, at the week 16
3. Markers of inflammation (CRP, calprotectin, cytokines and eicosanoids, thromboxanes) are measured by testing blood samples taken at baseline, at the week 6 and 12 of intervention and after wash-out period, at the week 16
4. Hormones in saliva (cortisol, aldosteron) are measured by testing saliva samples taken at baseline, at the week 6 and 12 of intervention and after wash-out period, at the week 16
5. Erythrocyte (Er) membrane fluidity is measured by spectrofuorimeter at baseline, at the week 6 and 12 of intervention and after wash-out period, at the week 16
6. Composition and content of serum fatty acids (FA) are measured by gas chromatography at baseline, at the week 6, 12 of intervention and after wash-out period, at the week 16
8. Length of DNA telomers in buccal cells is measured by qPCR at baseline and at 12 week intervention

Overall study start date
01/03/2013

Completion date
30/06/2020

Eligibility

Key inclusion criteria
1. Children and adolescents who met diagnostic criteria for depressive disorder or mixed anxiety and depressive disorder according to ICD 10
2. No signs of chronic somatic disease
3. Normal eating habits
4. Parents/guardians are willing to provide a signed informed consent
5. Children and adolescents are willing to provide blood, urine and saliva samples

Participant type(s)
Patient

Age group
Child

Lower age limit
10 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
60 = 30 in omega-3 group and 30 in omega-6 group

Total final enrolment
58

Key exclusion criteria
1. Chronic somatic diseases (endocrine, metabolic, autoimmune)
2. Dietary restrictions (vegetarians, lactose intolerance, celiac disease)
3. Psychotic disorders
4. Eating disorders
5. Addiction to psychoactive compounds
6. Personality disorders
7. Organic mental disorders
8. Pervasive developmental disorders

Date of first enrolment
01/03/2014

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
Slovakia

Study participating centre
Comenius University
Department of Paediatric Psychiatry, Faculty of Medicine, The National Institute of Children's Diseases
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Study participating centre
Comenius University
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Sponsor information

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Sponsor type
University/education

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ROR
https://ror.org/0587ef340

Funder(s)

Funder type
Research organisation

Funder Name
Slovak Research and Development Agency (Agentúra na Podporu Výskumu a Vývoja)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journals of papers discussing:
1. Clinical symptoms – results of pilot study - 2017
2. Markers of oxidative stress – pilot results -2017
3. Markers of inflammation – pilot results 2018
4. Fluidity of membranes and fatty acid composition - 2019
5. Telomere length – 2019
6. Mutual relation between clinical symptoms and markers of oxidative stress and inflammation - 2020

Intention to publish date
30/06/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from zdenka.durackova@fmed.uniba.sk and jana.trebaticka@fmed.uniba.sk

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Pilot study results	05/07/2017		Yes	No
Results article	Association of depression symptoms with levels of omega-3 and omega-6 fatty acids in serum	01/05/2020	18/03/2020	Yes	No
Results article	Lipid profile results	08/10/2020	22/10/2020	Yes	No
Results article	results for levels of thromboxane, brain-derived neurotrophic factor, homocysteine and vitamin D	27/03/2021	06/04/2021	Yes	No
Results article	Changes in stress hormones and markers of oxidative stress	10/08/2022	30/08/2022	Yes	No
Results article	The kynurenine and serotonin pathway, neopterin and biopterin in depressed children and adolescents: an impact of omega-3 fatty acids, and association with markers related to depressive disorder. A randomized, blinded, prospective study	13/02/2024	28/02/2024	Yes	No