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A Clinical Trial of Levocarnitine to Treat Autism Spectrum Disorders

Submission date	Recruitment status	[ ] Prospectively registered
20/03/2010	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
25/03/2010	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
16/08/2011	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
Autism-Carnitine Study#1

Study information

Scientific Title
A Prospective Double-Blind, Randomized Clinical Trial of Levocarnitine to Treat Autism Spectrum Disorders

Study objectives
The hypothesis tested in the present study was that blood carnitine levels in patients diagnosed with an ASD have a significant impact on behaviour, cognition, socialization, and health/physical

traits associated with an ASD diagnosis. The present prospective, double-blind, placebo controlled trial evaluated whether a standardized treatment regimen of liquid L-carnitine administered to patients diagnosed with an autism spectrum disorder (ASD) on a daily basis for 3-months would result in improved behaviour, cognition, socialization, and health/physical traits associated with an ASD diagnosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Liberty IRB, Inc. (Deland, Florida) approved on the 25th of September 2008 (ref: 08.09.0016)

Study design
Randomised double blind placebo controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Autism Spectrum Disorder (ASD)

Interventions
L-carnitine supplied in a liquid preparation by the Wellness Pharmacy (Birmingham, AL, USA) using a specific formula containing: 100 mg L-Carntine/mL with the inactive ingredients of methylcellulose, stevioside (stevia), tangerine flavour, and preserved water (containing methylparaben and propylparaben).
Placebos identical in appearance and taste to the active preparation, containing a 1% methylcellulose suspension with the inactive ingredients of stevioside (stevia), tangerine flavour, and preserved water (containing methylparaben and propylparaben).
A dose of 50 mg L-carnitine per Kg bodyweight per day (half the total dose administered in the morning and half the total dose administered in the evening) will be utilized in the present study with dosing calculated based on each participants intake weight.
The dosing regimen of the liquid preparation will be identical in both the L-carnitine and placebo groups, so that each study subject received a total of 0.5 mL per Kg of bodyweight per day (administered as 0.25 mL per Kg of bodyweight in the morning and 0.25 mL per Kg of bodyweight in the evening).
Study subject-specific dosing instructions will be placed on each liquid preparation provided to study subjects.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
L-carnitine

Primary outcome(s)

1. Childhood Autism Rating Scale (CARS)
Study participants will be evaluated using a CARS test conducted only by a single study investigator who observed the subjects and interviewed the parent(s), and was unaware as to the treatment status of the subject. The CARS test is a 15-item behavioural rating scale developed to identify autism as well as to quantitatively describe the severity of the disorder. The CARS test is a well-established measure of autism severity. The internal consistency reliability alpha coefficient is 0.94; the inter-rater reliability correlation coefficient is 0.71; and the test-retest correlation coefficient is 0.88. CARS scores have high criterion-related validity when compared to clinical ratings during the same diagnostic sessions, with a significant correlation of 0.84.
2. Autism Treatment Evaluation Checklist (ATEC)
Each study subject will be evaluated by their parents using an ATEC form. Parents will be unaware as to the treatment status of their child. The ATEC, designed by the Autism Research Institute (San Diego, CA, USA), is a one-page form. It consists of four subtests designed to measure the effects of treatment in persons with autism. The items are: (1) Speech/Language /Communication (14 items); (2) Sociability (20 items); (3) Sensory/Cognitive Awareness (18 items); and (4) Health/Physical/Behavior (25 items). The internal consistency reliability of the measure is high (0.94 for the Total score). The ATEC has been successfully used to measure treatment effects in autism.
3. Clinical Global Impression (CGI)
An overall CGI score will be collected by a single study investigator unaware of the treatment status of the study subject using a 3 point scoring system defined as follows: subject improved = 1, subject the same = 2, and subject worse = 3.
4. Hand Muscle Testing
Each subject will have their hand muscle strength tested using a pneumatic, adjustable squeeze pinch-gauge/dynamometer (Baseline Evaluation Instruments; White Plains, NY, USA) by a study investigator unaware of the treatment status of the subject. This instrument is a reliable and valid method for obtaining muscle force or torque measurements in children. Subjects will be tested using the smallest hand grasp bulb, and were given as many tries as needed to register their maximum grasp reading measured in kilopascals (kPa) for each hand. Special emphasis will be placed to ensure that the subject positioned the bulb in the palm of the hand and held the bulb in space to ensure that pressure was not applied by the study subject against a fixed surface. In addition, each study subject will be strongly encouraged by a study investigator to give maximum effort.

Key secondary outcome(s))

1. Treatment Adherence Measure (TAM) Form
A treatment adherence measure (TAM) form will be completed by the parents of each study subject. Parents will be unaware as to the treatment status of their child. The TAM is a ten-item self-report on treatment adherence that asks specific questions regarding the dose and frequency of use. The TAM was used to calculate the level of adherence to the treatment. It is a Morisky-type self-report adherence measure, designed to measure treatment adherence. Morisky-type adherence measures have been used widely, demonstrating good reliability as a self-report measure.
2. Side effects
2.1. Frequency and Intensity of Side Effect Rating (FISER)
2.2. Global Rating of Side Effect Burden (GRSEB)
2.3. Patient Report of Incidence of Side Effects (PRISE)
The FISER/GRSEB/PRISE forms will be completed by the parents of study subjects that will be unaware of the treatment status of their children. The FISER/GRSEB/PRISE forms include global

measures, each using a 7-point Likert-type scale rated 0-6, with one rating anchored for frequency, another rating the intensity of side effects encountered in the prior week that the study subject parents believed were due to the treatment, and the third asking the parents of study subjects to estimate the overall burden or degree of interference in day-to-day activities and function due to the side effects attributable specifically to the treatment. Frequency of side effects is rated as a percent time present: 0 = no side effects; 1 = present 10% of the time; 2 = 25% of the time; 3 = 50% of the time; 4 = 75%; 5 = 90%; and 6 = present all of the time. Intensity of side effects ranges from 0 = no side effects to 6 = intolerable side-effects. Impairment due to side effects ranges from 0 = no side effects to 6 = unable to function at all due to side-effects. The PRISE lists a variety of possible side effects from which to choose and a scale to rate the specific side effect. The measure also has a place to list any side effects not previously listed.
3. Lab testing
Study subjects will have lab testing collected at a Laboratory Corporation of American (LabCorp) draw station in the morning following an overnight fast. The lab will not be made aware of the treatment status of the study subjects. The procedures for collection and analysis were defined by LabCorp standard protocols (CLIA-approved). The following blood tests will be collected and evaluated on each study subject, including:
3.1. Whole blood white blood cell count (WBC)
3.2. Whole blood red blood cell count (RBC)
3.3. Whole blood platelet count
3.4. Serum creatinine
3.5. Serum blood urine nitrogen (BUN)
3.6. Serum alkaline phosphatase
3.7. Serum aspartate aminotransferase (AST/SGOT)
3.8. Serum alanine aminotransferase (ALT/SGPT)
3.9. Serum glucose
3.10. Serum carnitine (total and free)

Completion date
31/12/2009

Eligibility

Key inclusion criteria
1. Subjects diagnosed with an ASD
2. Aged from 3 to 10 yrs-old (males and females)
3. Study subject bodyweights between 13.2 Kg to 40.4 Kg

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
3 years

Upper age limit

10 years

Sex
All

Key exclusion criteria
1. No study subject previously received carnitine-based therapy or previous methionine or lysine supplementation
2. No study subject had any change in therapy or treatment (including medications) within 1 month prior to the study

Date of first enrolment
01/01/2009

Date of final enrolment
31/12/2009

Locations

Countries of recruitment
United States of America

Study participating centre
14 Redgate Ct
Silver Spring
United States of America
20905

Sponsor information

Organisation
Autism Research Institute (USA)

ROR
https://ror.org/01xsmpb09

Funder(s)

Funder type
Research organisation

Funder Name

Autism Research Institute (USA)

Funder Name
CoMeD, Inc. (USA)

Funder Name
The Institute of Chronic Illnesses, Inc. (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration