ORIGINAL ARTICLE

Behavioral Benefits of Camel Milk in Subjects with Autism Spectrum Disorder

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ABSTRACT

Objective: To investigate the possible therapeutic effects of camel milk on behavioral characteristics as an interventional strategy in autistic children.

Study Design: Double-blind, Randomized Clinical Trial (RCT).

Place and Duration of Study: Autism Research and Treatment Center, Al-Amodi Autism Research Chair, Department of Physiology, Faculty of Medicine, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia, from October 2012 to May 2013.

Methodology: Changes in behavioral characteristics in 65 (boys=60, girls=5) children with autism (aged from 2 to 12 years) were assessed. The behavioral symptoms were evaluated by Childhood Autism Rating Scale (CARS), Social Responsiveness Scale (SRS), and Autism Treatment Evaluation Checklist (ATEC) before and after the 2 weeks of camel milk therapy.

Results: Significant differences were detected on Autism Spectrum Disorder (ASD) by CARS, SRS and ATEC scales, following 2 weeks of camel milk consumption, but not in the placebo group.

Conclusion: The present study demonstrates that camel milk could be very promising therapeutic intervention in ASD. Further wide scale studies are strongly recommended.

Key Words: *Autism spectrum disorder (ASD). Camel milk. Behavioral symptoms.*

INTRODUCTION

Autism Spectrum Disorders (ASDs) are a wide range of neurodevelopmental conditions that demonstrate considerable phenotypic heterogeneity, both in terms of presentation at any one age and across development. The current classification systems include three domains of difficulties: reciprocal social interaction, abnormalities in communication, and patterns of nonfunctional restricted, repetitive and stereotyped behaviors.[1] Although there is no known unique cause of autism, there is growing evidence that autism can be caused by a variety of factors including autoimmunity[2] originated by dairy food allergy. While several intervention methods for ASDs have been used to treat children with autism spectrum disorders, very few have been subjected to careful scientific investigation.

Autoimmunity to CNS was also documented by several research groups, through the presence of brain specific auto-antibodies in the brains of some autistic children.[3] The reason behind the formation of some brain auto-antibodies in some patients with autism is not fully understood. It is speculated that an autoimmune reaction to neurons might be triggered by some cross-reacting antigens in the environment resulting in the release of neuronal antigens. These neuronal antigens may result in induction of autoimmune reactions through the activation of the inflammatory cells in genetically susceptible individuals. The environmental antigens may include food allergies to certain peptides such as gliadin, cow's milk protein and soy.[4]

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Camel milk has emerged to have potential therapeutic effects in diseases such as diabetes,[5] and hepatitis B,[6] as well as cow milk allergy in children.[4] Children with severe food allergies improved rapidly with camel milk.[7] It contains various 'protective proteins' (Lysozymes, Immunoglobulins, Lactoferrin, Lactoperoxidase, Peptidoglycan Recognition Protein (PGRP) and N-acetyl-§-glucosaminidase (NAGase); mainly enzymes which have antiviral, antibacterial and immunological properties.[7]

Recently, Bashir and Al-Ayadhi investigated[8] the role of the effectiveness of camel milk (raw and boiled) on Thymus and Activation-Regulated Chemokine (TARC) serum levels and CARS score in subjects with autism and compared to placebo group (cow milk). The results suggested that camel milk therapy over the course of two weeks, significantly decreases the serum levels of TARC among the study subjects and also improve clinical measurements of ASD severity (CARS score).

The above findings initiated the authors' interest to test the effectiveness of camel milk on behavioral changes in subjects with Autism Spectrum Disorders. The hypothesis tested in the present study was that autism can be caused by food allergy.[9] It has been believed that normal diary food is harmful to the immune system, brain and bodies of children with ASD[10] and have a significant impact on behavior, cognition, socialization, and health/physical traits associated with an ASD diagnosis. The present prospective, double-blind, placebo controlled trial has evaluated whether a standardized treatment of camel milk administered to patients diagnosed with ASD on a daily basis for 2 weeks would result in improved behavior, cognition, socialization, and health/physical traits associated with an ASD diagnosis.

METHODOLOGY

The study was a double-blinded, Randomized Clinical Trial (RCT) conducted at Autism Research and Treatment Center, Al-Amodi Autism Research Chair, Department of Physiology, Faculty of Medicine, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia, from October 2012 to May 2013.

Autistic children with typical symptoms, especially those with known allergies or food intolerances, were randomly recruited in this study. The patients were referred by neuropediatric clinics from all around the Kingdom of Saudi Arabia. This study protocol received the ethical approval from the Institutional Review Board of King Saud University, Faculty of Medicine. Participants were given a complete description of the study and a written informed consent was obtained from all parents/guardians before they were enrolled in the study.

The inclusion criterion for the autism group was meeting the cut-off score of the Autistic Disorder based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria.[1] All participants were screened via parental interview for current and past physical illnesses. Subjects were excluded from the investigation, if they had dysmorphic features or diagnosis of fragile x or other serious neurological (e.g., seizures), psychiatric (e.g., bipolar disorder) or known medical conditions. Children with known endocrine, cardiovascular, pulmonary, and liver or kidney disease were also excluded from the study.

The participants were randomly divided into three groups: Group I (n=25) received pasteurized camel milk; Group II unpasteurized camel milk (n=22) and Group III received cow milk as a placebo (n= 18). All groups received the same instructions, volume of milk and containers to preserve the blinding of the study.

Parents were instructed to include an average of 500 ml of camel milk in their children's regular daily diet for a period of 2 weeks. Parents were asked to continue with the children's daily routines. They were not allowed to add or remove any interventions such as diet plans, supplements or pharmacotherapies throughout the study period. It was also instructed to drink cold milk, beginning with small quantities and increase gradually until 500 ml per day to avoid any risk of diarrhea.

ARTC psychologist assessed the disease severity through baseline psychology scales including Childhood Autism Rating Scale (CARS),[11] Social Responsiveness Scale (SRS)[12] and Autism Treatment Evaluation Checklist (ATEC).[13]

Medical history of the child and family was obtained through a structured questionnaire interview conducted with the parents/legal guardians. Height and weight of the patients were recorded. During the study period, the patients' progress were monitored by phone calls. After 2 weeks, the participants returned for a follow-up where all psychology scales were conducted. All observations by parents were also noted. Safety evaluations including physical examinations were carried out by the prime investigator for patients who showed any negative symptoms.

Fresh camel milk was obtained by ARTC from a trusted camel farm who ran regular routine veterinary checkups on the camels. After receiving the milk, microbiological screening tests were conducted on all milk batches to ensure that it was free of pathogens commonly found in raw camel milk.[14] The pathological screenings were conducted to detect Campylobacter, Bacillus cereus enterotoxin, *E. coli* O157:H7, Listeria, Salmonella by GLISA rapid testing using the kits Singlepath Campylobacter, Doupath Cereus Enterotoxin (EMD chemicals), Reveal *E. coli* O157:H7, Salmonella, Listeria (Neogen) and B. Brucela (Anigen). Any batch tested positive for the above mentioned pathogens was immediately excluded from the above study. Camel milk supplied to Group I was pasteurized by heating to 65°C for 15 seconds, then removed, cooled in a ice pot initially and then stored in the freezer at -80°C. Milk supplied to Group II was not heated to avoid losing beneficial nutrients and proteins.[15] Frozen milk was supplied to patients using BPA-free freezer bottles and thawed on countertops as needed.

The data were prospectively collected, analyzed and results were presented as mean ± SD (standard deviation). Statistical differences in scores in each scale CARS, SRS, and ATEC before and 2 weeks after milk therapy were determined by means of paired sample t-test with $p \leq 0.05$ considered as significant.

RESULTS

There were a total of 65 children including 60 males and 5 females. Changes in behavioral characteristics in 65 (n=65) subjects with autism aged 2 - 12 years, mean = 7.8 years, were assessed. The behavioral symptoms were evaluated before and after 2 weeks of milk consumption period, by the CARS, SRS and ATEC in three groups of autistic children having a clinical diagnosis by (DSM-IV).[1] The lower the scores are, the less severe the symptoms are. Changes in all measures of symptoms of autism over the course of the study are shown in Tables I - III.

Table I shows the CARS evaluations scoring system which illustrates statistically significant changes in the raw camel milk group (mean score before = 37.6 ±6.3, after = 34.5 ±5.2, p=0.004), and the boiled camel milk group (mean score before =37.1 ±3.6, after = 33.8 ±4.9, p=0.0001). Furthermore, there were no significant changes in the placebo group (mean score before = 34.2 ±3.3, after = 33.8 ±3.5, p=0.41). These changes represented reductions of 8% and 9% in each raw and boiled camel milk . However, no significant change was observed in cow milk as far as CARS score is concerned.

SRS mean score for all groups along with each subscale was calculated (Table II). The SRS evaluations showed statistically significant changes in mean SRS subscale scores in social cognition (p=0.002), social communication (p=0.018) and social awareness (p=0.050), for the raw camel milk group. On the other hand, the boiled camel milk group demonstrated a significant change only in social cognitions subcategory (p= 0.0001). No significant change in placebo group was observed.

The ATEC (mean ± SD) scores of different categories of camel milk (raw and boiled) and placebo groups are shown in Table III. The ATEC evaluations showed that ATEC total and subscale scores in different categories do not show significant changes in camel milk groups (raw and boiled) compared to the placebo group except speech/language/communication in boiled camel milk group (p=0.0001).

Table I: Change in clinical outcome measures in CARS scores in autistic children.

	Score before therapy Mean ± SD	Score after therapy Mean ± SD	p-value
Raw camel milk	37.6 ± 6.3	34.5 ± 5.2	0.004*
Boiled camel milk	37.1 ± 3.6	33.8 ± 4.9	0.0001*
Placebo (cow milk)	34.2 ± 3.3	33.8 ± 3.5	0.41

**significant*

DISCUSSION

Upto date there is no known effective approved intervention method for autism spectrum disorders. Consequently, this creates many challenging issues and it has become an area of a major controversy. Over the last few years, a number of research groups suggested possible autoimmunity as a significant etiological factor in autism.[16]

This study represents the first prospective study on the use of camel milk as potential therapeutic intervention strategy for children with autism. In this study, camel milk (both boiled and raw) demonstrated significant effect on some autistic behaviors, through improvement in social cognition, social communication, and social awareness (SRS). Furthermore, boiled camel milk produced significant improvement in speech/language/ communication (ATEC). This was supported by the significant changes in the CARS scoring results. Camel milk with its unique characters could be a promising therapeutic intervention strategy in autism spectrum disorders.

Table II: Change in clinical outcome measures in SRS scores in the autistic children.

Sub Scales	Raw camel milk			Boiled camel milk			Placebo (cow milk)		
	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value
Social cognition	75 (4.3)	70 (5.3)	0.002*	75 (3.8)	70 (4.1)	0.0001*	78 (7.2)	72 (7.5)	0.437
Social communication	72 (5.7)	70 (6.6)	0.018*	71 (5.5)	68 (5.5)	0.076	75 (9.0)	73 (5.3)	0.722
Social motivation	74 (6.5)	73 (4.0)	0.301	73 (4.9)	72 (19)	0.482	75 (6.1)	74 (5.1)	0.225
Autistic mannerism	78 (7.1)	78 (7.4)	0.219	78 (6.4)	75 (20)	0.073	82 (8.0)	79 (9.8)	0.423
Social awareness	71 (5.4)	70 (5.4)	0.050*	72 (5.1)	72 (5.8)	0.650	79 (8.3)	67 (5.0)	0.113
Average	75 (6.2)	74 (6.3)	0.037*	75 (5.0)	73 (5.0)	0.033*	81 (8.5)	75 (8.1)	0.104

**significant*

Table III: Change in clinical outcome measures in ATEC subscales scores in autistic children.

Sub Scales	Raw camel milk			Boiled camel milk			Placebo (cow milk)		
	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value	Score before therapy Mean ± (SD)	Score after therapy Mean ± (SD)	p-value
Speech/language/ communication	4.6 (6.1)	3.5 (3.0)	0.200	7.6 (7.9)	6.2 (6.8)	0.012*	10 (7.0)	12 (8.4)	0.548
Sociability	23 (6.3)	21 (3.7)	0.061	21 (6.4)	21 (8.4)	0.790	23 (7.9)	22 (4.9)	0.430
Sensory/cognition/ awareness	24 (7.3)	21 (5.5)	0.131	23 (8.8)	21 (12)	0.132	24 (8.3)	24 (6.6)	0.838
Health/physical/ behavior	24 (7.3)	22 (5.2)	0.120	21 (9.1)	20 (6.1)	0.405	24 (8.4)	23 (5.4)	0.421
Total	74 (15)	72 (10)	0.566	70 (16)	69 (18)	0.838	80 (14)	76 (13)	0.156

**significant*

Since recent reports demonstrated higher oxidative stress statues in ASD subjects compared to normally developing controls[17], it makes camel milk an ideal antioxidant food. Furthermore, camel milk can certainly play important role in the prevention of diary food allergies and has been used to treat children with autism.[7] However, to date; few studies reported some improvements in symptom scores in children who were treated with camel milk.[18,19]

A significant therapeutic effect of raw camel milk is decreased on boiling even on pasteurization.[20] Camel milk has good bacterial and anti-viral activity thus if is used raw, there are less chances of transmission of infection. This concept is consistent with the historic belief that natural substances play an important role in preventative and therapeutic treatment.[20]

Milk protein casein plays important role in the food allergies related disorders and cause autism.[18] Many children with autism may have gastrointestinal difficulties that make it hard for them to digest milk protein properly. There are different possibilities for ways in which this could affect children with autism. This could be through the unique immunological properties of camel milk immunoglobulins (Igs) including unique subclasses IgG2 and IgG3, contribute to camel milk's incredible infection fighting and eradication capacity. Camel Igs being so small are able to penetrate into tissues and cells to completely neutralize the enzyme activity of an infectious agent such as a bacteria or virus whereas, human antibodies Igs cannot.[21] Second possibility, is through the strong antioxidant properties of camel milk.[22] Bioactive peptides derived from camel milk protein showed higher functionality including antioxidant activity, anti-hypertension effect and antimicrobial activity comparing to bioactive peptides from bovine milk proteins.[23] Last but not the least, it is a fact that camel milk does not contain allergens like beta-lactoglobulin and a “new” beta-casein which are present in cow milk and thus makes the camel milk attractive for children suffering from milk allergies.[7] Another relevant fact is that the components of camel milk include immuno-globulins similar to those in mothers' milk, which reduce children's allergic reactions and strengthen their future response to foods. The beta-casein in camel milk is completely a different protein due to the amphipathic structure; so it has a strong inherent tendency to self-associate into micelles of 15 - 60 molecules. Association and conformational changes can have a major influence on the function of beta-caseins.[24]

Casein molecules are actually micelles and camel milk micelles have been found to be larger in size (15 nm) than those of cow milk or human milk. Camel milk has a lower pH than other milk, so upon entering the stomach the casein micelles do not breakdown into casein and, therefore, do not break into casomorphins. Casomorphin creation from cow milk consumption is a common problem in autism that increases autistic symptoms.[25]

Further studies are needed by other investigators to confirm these findings; however, in the light of the positive results of this study and those of several previous studies,[18,19] the use of camel milk appears to be a promising treatment for children with autism. Camel milk therapy was safe and well-tolerated. None worsened and no side effects were reported.

CONCLUSION

Autism is a severe, lifelong disorder with serious emotional and financial consequences. Its incidence is rapidly increasing, and its etiology is still unclear. The present study demonstrates that camel milk could be very promising therapeutic intervention in ASD. Further wide-scale studies are strongly recommended.

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