Donkey milk-based formula: A substitute for patients with cow’s milk protein allergy

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ABSTRACT
Cow’s milk protein allergy affects 2-7% of children using cow’s milk formulae. Fifty to eighty percent of them develop allergy to other food items and substitutes. On the search for a safe and affordable substitute, we reviewed the composition of milks of the domestic mammals in close contact with man. Milk constituents studied included fat, protein, lactose, minerals, water, pH, specific gravity and caloric value. Compared to others, donkey milk was found to be closest to breast milk when the amount of 16ml of sunflower is added to one liter of this milk. To our knowledge, no allergy to donkey milk has been reported yet.

Key words: Donkey; Cows; Milk; Composition; Allergy; Sunflower oil; Substitute.

INTRODUCTION
Food Allergy (FA) is defined as an immunologically mediated adverse reaction to food stuff. It may present as a generalized reaction where the offending substance is ingested, absorbed, passed to the portal circulation and thence to the whole body. Localized allergic reactions develop as a result of activation of the mast cells by the offending substance, local formation of immune complex and local lymphocyte-mediated cytotoxicity. General incidence of allergy is about 13%, it is doubled when one parent of the affected child is allergic and tripled when both parents are affected [1, 2]. Cow’s milk protein allergy (CMPA) is one of the most common food allergies in infants. It affects 2 – 7% of children less than 6 month of age. It may present as an immediate IgE-mediated hypersensitivity reaction where degranulation of the mast cells leads to liberation of histamine, 5-Hydroxytryptamine (5HT), prostaglandin E2 (PGE2) and a consequent gross morphological and physiological changes in the affected organ. This is best exemplified in anaphylactic reactions, eosinophilic gastroenteritis, urticaria, eczema, rhinoconjunctivitis, angioedema, asthma and migraine. Delayed non-IgE-mediated reaction is characterized by lymphocyte infiltration and secondary destructive lesions as seen in enteropathy, enterocolitis, Heiner’s syndrome, type 1 diabetes mellitus and infantile colic.

Clues to the diagnosis of FA and CMPA include a positive family history, appearance of symptoms soon after ingestion of the offending substance, atopy during the first year of life and perioral rash or urticaria on spilling.

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How to cite this article:
Clinical diagnosis is possible by Elimination-Challenge tests though confirmation should be done by laboratory tests that include eosinophil count, IgE and other specific antibodies level assay, radioallergosorbent test (RAST) and Skin Prick test. However, invasive procedures e.g. jejunal biopsy may be needed in certain conditions.

Management of CMPA includes desensitization of the allergic patient with intra-dermal or sublingual introduction of a diluted amount of the offending protein, use of soya bean milk, milk from other mammals, meat-based formulae and casein and whey hydrolysate formulae as substitute. However, availability, cost, contaminants and cross reactions limited the use of these substitutes [4].

The most recent approach to ameliorate allergic manifestations in cases of FA is the use of 4 basic DNA-based immunotherapy methods [5]. These are:

a- Gene vaccine
b- Allergen mixed with immune-stimulatory oligodeoxynucleotide
c- Physical conjugates of allergens with oligodeoxynucleotide
d- Immunomodulation with oligodeoxynucleotide alone.

However, results of clinical trials with these modalities are yet to be published and evaluated.

The main objective of this study was to define a substitute formula for children with CMPA that is nutritionally adequate, safe, with good taste and smell, non-immunogenic and available at affordable price.

**MATERIAL AND METHODS**

A thorough net and literature search was carried out to evaluate and compare the results of studies done on analysis of milk from domestic animals that are in close contact with man including cows, buffalos, camels, goats, sheep, mares and donkeys. Milk constituents studied included fat, protein, lactose, minerals, water, pH, Specific gravity and calorific value. All were compared to breast milk and cost was estimated according to local measures.

An average of each constituent from the most recent studies is included.

**RESULTS**

Compared to breast milk (Table 1), fresh cow’s milk has low pH, high protein, high minerals and low lactose. Buffalo milk has low pH, high fat and minerals and low protein and lactose. Goats and sheep milk have low pH, very high protein, mineral and fat content especially in sheep where a high caloric value is scored. Camel’s milk has low pH, high fat, protein and minerals and low lactose. Mare’s milk has low pH, high protein and minerals and low fat and caloric value. Donkey’s milk has the same pH as breast milk, less fat and caloric value and a slight increase in protein and minerals (Table 1). Adding 1.6 gm of sunflower oil to 100 ml of donkey milk (16ml/L) compensates for the low fat and caloric values found in donkey milk and constitutes a formula that is very close to breast milk (Table 2).

| Table 1- Composition of milk of mammals (gm/dl) |
|---------|--------|--------|--------|--------|--------|--------|--------|--------|
| Fat     | 3.6    | 3.9    | 6.6    | 3.8    | 7.3    | 4.9    | 2.1    | 2.0    |
| Protein | 1.2    | 3.3    | 0.6    | 3.9    | 5.7    | 3.5    | 1.7    | 1.5    |
| Lactose | 6.4    | 4.3    | 4.7    | 4.7    | 4.6    | 5.0    | 6.2    | 6.3    |
| Minerals| 0.2    | 0.6    | 0.7    | 0.8    | 0.8    | 0.8    | 0.5    | 0.4    |
| Water   | 88.6   | 87.9   | 87.4   | 86.8   | 81.6   | 85.8   | 89.5   | 89.8   |
| pH      | 7.1    | 6.5    | 6.7    | 6.5    | 6.5    | 6.5    | 6.7    | 7.1    |
| SG      | 1.03   | 1.03   | 1.03   | 1.03   | 1.03   | 1.03   | 1.03   | 1.03   |
| Calories| 63     | 66     | 81     | 69     | 107    | 78     | 50     | 49     |

SG - specific gravity

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Table 2 – Milk composition after adding sunflower oil to donkey milk (gm/dl)*

<table>
<thead>
<tr>
<th></th>
<th>Breast</th>
<th>Donkey</th>
<th>Donkey+ sunflower oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>3.6</td>
<td>2.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Protein</td>
<td>1.2</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Lactose</td>
<td>6.4</td>
<td>6.3</td>
<td>6.3</td>
</tr>
<tr>
<td>Minerals</td>
<td>0.2</td>
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<tr>
<td>Calories</td>
<td>63</td>
<td>49</td>
<td>63.4</td>
</tr>
</tbody>
</table>

SG: specific gravity
*1.6 gm of sunflower oil to 100 ml of donkey milk (16ml/L)

Table 3 - Sunflower oil contents

1- Polyunsaturated fatty acids: Omega 3, 6, 7 and 9.
2- Vitamins: A, B1, B2, B3, B5, B6, D, E and K.
3- Minerals: Calcium, Phosphorus, Copper, Magnesium, Manganese, Selenium and Iron.
4- Amino acids: Aspartic acid, Threonine, Serine, Glutamic acid, Glycine, Alanine, Cystine, Valine, Methionine, Isoleucine, Leucine, Tyrosine, Phenylalanine, Histadine and Lysine.

DISCUSSION

Cow’s milk protein allergy affects 2-7% of children, 25-80% of them have cross sensitivity to the currently used substitute formulae including goats, sheep, soya bean milks and milk hydrolysate. Goat’s milk is known to be deficient in folic acid as well as its liability to transmit diseases like brucellosis. Camel milk is homogeneous i.e. foremilk has the same amount of fat as the hind milk, yet its water content is not constant and has seasonal variations. Mare’s milk is relatively expensive and contains high levels of contaminants e.g. pesticides and dioxides. Donkey milk, in contrast, is the closest to breast milk [8-12] except for the low fat content and low calorific value which can be compensated for by adding sunflower oil. It is cheap and has sweat taste. It is easily digestible because of its high whey content compared to casein. It contains low average number of somatic cells, low bacterial count and does not carry bovine diseases. It has been used by Hippocrates as a remedy in treatment of arthritis, cough, surgical wounds and ulcers. Queen Cleopatra of Egypt used it as a bath to keep her skin soft and moist. Avicenna advised using it to strengthen teeth and in treatment of cough, haemoptysis, ulcers, wounds and ascites [13]. It is currently used in Sudan as a native medicine to treat whooping cough and in India to treat chikungunya, probably because of its high immunoglobulin content. In France and Italy it is used as a substitute and in manufacture of beauty soaps and creams. It is not
subject to tuberculosis and can be preserved for a long time when frozen.

Sunflower oil is a safe, palatable and relatively affordable in the amounts mentioned above [14]. It is formed of polyunsaturated fatty acids (75% linoleic acid), thus it helps lowering blood cholesterol. It contains vitamins, minerals, essential amino acids and volatile oils (Table 3). It is noteworthy that most recently, the use of unmodified donkey’s milk was associated with growth impairment and nutritional deficiencies in a 5-month cow’s milk-allergic infant [15]. Unmodified donkey’s milk has a poor lipid content and a low caloric value in addition to a very low iron content.

In conclusion, low pH, high solute and contaminant content, cost, cross sensitivity and transmission of diseases are limiting factors to use milk of most of the domestic animals as substitute in patients with CMPA. In contrast, donkey milk with an addition of 16 ml sunflower oil per liter is found to be closest to breast milk and the best substitute to cow’s milk. To our knowledge, no allergy to donkey milk has been reported yet.

REFERENCES

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