of this population when compared to the normal infants, the ability to provide the extra calories is an important step toward therapeutic intervention in the nutritional management of pre and post-surgical infants.

[0008] Thus, a nutritional solution is needed to prepare and assist infants in recovery from surgery, particularly those who must maintain a fluid restricted diet.

SUMMARY

[0009] The current disclosure provides a high energy/high fat human milk composition that can be administered orally or enterally to increase the caloric content of human donor milk or mother's own milk while not substantially increasing the overall volume or osmotic load necessary to meet the nutritional requirements of these infants. The opportunity for an exclusive human milk diet in infants requiring surgery thereby improves short and long term clinical outcomes including improved growth velocity and wound healing resulting in a decreased length of hospital stay (LOS) and improved neurodevelopment.

[0010] This disclosure features human milk compositions and methods of making and using such compositions. In some examples the human milk composition is a human milk fortifier. In some examples, the human milk composition comprises milk and human milk fortifier. In some examples, the milk is human mother's milk. In other examples, the milk is pooled human milk. In some examples, the milk is a ready-to-feed product. In other examples, the milk is non-human. In some examples, the human milk composition comprises infant formula.

[0011] The present disclosure provides human milk compositions comprising from about 19 mg/mL to about 26 mg/mL protein, from about 49 mg/mL to about 64 mg/mL fat, and from about 81 mg/mL to about 97 mg/mL carbohydrates. In another example, the human milk composition comprises about 24 to about 26 mg/mL protein, from about 60 mg/mL to about 64 mg/mL fat, and from about 83 mg/mL to about 97 mg/mL carbohydrates. In another example, the human milk composition comprises about 19 to about 20 mg/mL protein, from about 49 mg/mL to about 51 mg/mL fat, and from about 81 mg/mL to about 89 mg/mL carbohydrates. In another example, the human milk composition comprises about 21 to about 23 mg/mL protein, from about 54 to about 57 mg/mL fat, and about 82 to about 89 mg/mL carbohydrates.

[0012] In one example, the method provides administering to a subject a human milk composition comprising from about 19 mg/mL to about 26 mg/mL protein,

from about 49 mg/mL to about 64 mg/mL fat, and from about 81 mg/mL to about 97 mg/mL carbohydrates. In another example, the method provides administering to a subject a human milk composition comprising about 24 to about 26 mg/mL protein, from about 60 mg/mL to about 64 mg/mL fat, and from about 83 mg/mL to about 97 mg/mL carbohydrates. In another example, the method provides administering to a subject a human milk composition comprising about 19 to about 20 mg/mL protein, from about 49 mg/mL to about 51 mg/mL fat, and from about 81 mg/mL to about 89 mg/mL carbohydrates. In another example, the method provides administering to a subject a human milk composition comprises about 21 to about 23 mg/mL protein, from about 54 to about 57 mg/mL fat, and about 82 to about 89 mg/mL carbohydrates.

[0013] In one example, the human milk composition provides from about 67 to about 139 kcal/kg/day. In another example, the human milk composition provides from about 80 to about 130 mL/kg/day. In another example, the human milk composition provides from about 90 to about 100 mL/kg/day.

[0014] In one example, the human milk composition further comprises one or more constituents selected from the group consisting of: calcium, chloride, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc. In another example, the human milk composition further comprises human milk oligosaccharides.

[0015] In one example, the human milk composition is administered to the subject orally. In another example, the human milk composition is administered to the subject enterally.

[0016] In one example, said subject is a human child, or infant. In a particular example, the child is from about 18 years old to about 2 years old. In other examples, said subject is a child about two years old or younger. In another example, said subject is less than or equal to 7 days old. In still other examples, said subject is a premature infant. In some examples, said subject is a human adult. In one example, the human adult is 18 years old or older.

[0017] In one example, the method comprises providing nutrition to a subject who is undergoing or has undergone surgery. In a further example, the method comprises administering to a subject a human milk composition comprising a fortifier composition. In one example, the human milk composition provides about 70% of the total nutrition and the fortifier composition provides about 30% of the total nutrition. In another example, the human milk composition provides about 60% of the total nutrition and

the fortifier composition provides about 40% of the total nutrition. In another example, the human milk composition provides about 50% of the total nutrition and the fortifier composition provides about 50% of the total nutrition.

[0017a] In one aspect, the disclosure provides use of a human milk fortifier composition comprising a human protein constituent from about 35 to about 45 mg/ml and a human fat constituent from about 80 to about 100 mg/ml for the manufacture of a medicament for providing nutrition to a subject who is about to undergo or has undergone surgery, wherein the subject is a full-term infant.

[0017b] In one aspect, the disclosure provides use of a fortified human milk composition for the manufacture of a medicament for providing nutrition to a subject who is about to undergo or has undergone surgery, wherein the fortified human milk composition comprises human milk and human milk fortifier; wherein the fortified human milk composition comprises a human protein constituent from about 10 to about 30 mg/ml protein and a human fat constituent from about 40 to about 70 mg/ml fat; and wherein the subject is a full-term infant.

[0018] Human milk is defined as expressed breast milk or donor milk and its derivatives, human milk-based fortifier and human milk caloric fortifier. Standard human milk formulation include Prolact-RTF™, PROLACTPLUS™ PROLACT+4®, PROLACT+6®, PROLACT+8®, and/or PROLACT+10®, which are produced from human milk and contain various concentrations of nutritional components.

[0019] The disclosure features standardized human milk formulations or fortifiers, which are produced from human milk. Methods of making and using such compositions are also described herein. In some examples, standardized human milk formulations are supplemented with vitamins and/or minerals. In some examples, the standardized milk formulations are fed orally to subjects who are undergoing or have undergone surgery. The methods of generating these compositions are designed to optimize the amount of nutrients and calories in the compositions.

[0020] In some examples, the human milk compositions further comprise one or more constituents selected from the group consisting of: calcium, chloride, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc.

[0021] In one example, the disclosure features a human milk fortifier composition comprising: a human protein constituent from about 35 mg/mL to about 45 mg/mL and a human fat constituent from about 80 mg/mL to about 100 mg/mL. In one example, the disclosure features a human milk fortifier composition comprising: a human protein constituent from about 35 mg/mL to about 42 mg/mL and a human fat constituent from about 84 mg/mL to about 95 mg/mL. In another example, the disclosure features a human milk fortifier composition comprising: a human protein constituent of about 37 to about 42 mg/mL and a human fat constituent of about 86 to about 94 mg/mL. In another example, the disclosure features a human milk fortifier composition comprising: a human protein constituent of about 39.2 mg/mL and a human fat constituent of about 94.5 mg/mL. The carbohydrate constituent can include additional lactose. In some examples, the composition further comprises one or more constituents selected from the group consisting of: calcium, chloride, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc.

[0022] In one example, a method for obtaining a human milk composition is provided. In some examples, the method includes: (a) genetically screening human

milk for one or more viruses; (b) optionally filtering the milk; (c) optionally heat-treating the milk, e.g., at about 63°C or greater for about 30 minutes; (d) separating the milk into cream and skim; (e) adding a portion of the cream to the skim; and (f) pasteurizing or otherwise sterilizing the composition.

[0023] In some examples, the genetic screening in step (a) is polymerase chain reaction and/or includes screening for one or more viruses, e.g., human immunodeficiency virus Type 1 (HIV-1), hepatitis B virus (HBV), and/or hepatitis C virus (HCV).

[0024] In some examples, the milk is optionally filtered through an about 200-micron screen in step (b).

[0025] In some examples, the method further includes running cream, e.g., about 30-70% fat in the cream, through a separator following step (d). In one example, the method further includes filtering the skim through filters after step (d), e.g., to filter the water out of the skim. In some examples, after filtering the skim after step (d), the filters used in the filtering is washed to obtain a post wash solution. In further examples, the post wash solution is added to the skim.

[0026] In some examples, the method further includes carrying out mineral analysis of the portion of the composition obtained after step (e). In one example, the method also includes adding to the composition obtained after step (e) one or more minerals selected from the group consisting of: calcium, chloride, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc. Adding of the one or more minerals includes heating the composition, in some examples.

[0027] In a particular example, the method also includes cooling the composition after step (f), carrying out biological testing of a portion of the composition after step (f), and/or carrying out nutritional testing of a portion of the composition after step (f).

[0028] In some examples, the human milk of step (a) is pooled human milk. Thus, in some examples, the methods provided herein are carried out with large volumes of the starting material, e.g., human milk, e.g., pooled human milk. In some examples, the volumes can be in the range of about 75 liters/lot to about 10,000 liters/lot of starting material (e.g. about 2,500 liters/lot or about 2,700 liters/lot or about 3,000 liters/lot or about 5,000 liters/lot or about 7,000 liters/lot, about 7,500 liters/lot or about 10,000 liters/lot).

[0029] In another example, the disclosure features a method for obtaining a human milk composition. The method includes: (a) genetically screening human milk for one or more viruses; (b) filtering the milk; (c) adding cream; and (d) pasteurizing.

[0030] In one example, the genetic screening in step (a) is a polymerase chain reaction. In some examples, the genetic screening includes screening for one or more viruses, e.g., HIV-1, HBV, and/or HCV.

[0031] In one example, the milk is optionally filtered through an about 200 micron screen in step (b). In some examples, the method further includes ultra-filtering the whole milk after step (b) through filters. In some examples, the filters used during ultra-filtering are post washed. In some examples, the filters used during ultra-filtration are post washed with permeate. In some examples, the filters used during ultra-filtration are post washed with water.

[0032] In some examples, the composition is cooled after step (d). In some examples, biological and/or nutritional testing of the composition is carried out after step (d).

[0033] In some examples, the human milk of step (a) is pooled human milk. Thus, in some examples, the methods featured herein are carried out with large volumes of the starting material, e.g., human milk, e.g., pooled human milk. In some examples, the volumes are in the range of about 75-10,000 liters/lot of starting material. In a particular example, the volume is about 2,000 liters/lot. In another example, the volume is about 2,500 liters/lot. In another example, the volume is about 2,700 liters/lot. In another example, the volume is about 3,000 liters/lot. In another example, the volume is about 4,000 liters/lot. In still another example, the volume is about 5,000 liters/lot. In still another example, the volume is about 7,000 liters/lot. In still another example, the volume is about 7,500 liters/lot. In still another example, the volume is about 10,000 liters/lot.

[0034] In some examples, the method includes adding to the composition obtained after step (c) one or more minerals selected from the group consisting of: calcium, chloride, copper, iron, magnesium, manganese, phosphorus, potassium, selenium, sodium, and zinc.

[0035] In one example, a method is provided for improving one or more clinical outcomes subjects recovering from surgery. In some examples, the one or more improved clinical outcomes comprise short and/or long term benefits. In certain examples, the one or more improved clinical outcomes are selected from improved

neurodevelopmental outcomes, improved growth velocity including rate of weight gain, incremental linear growth, incremental rate of head circumference growth, reduced length of stay in the hospital and a reduction of the days of parenteral nutrition. In some examples, the one or more improved clinical outcomes is selected from reduced incidence and/or severity of feeding intolerance, reduced incidence and/or severity of sepsis, reduced incidence and/or severity of necrotizing enterocolitis (NEC), rediced incidence and/or severity of wound infections, and/or wound dehiscence. Thus, in one example, methods for improving the clinical outcome of subjects, particularly infants, recovering from surgery is provided.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] Figure 1 is a flow chart showing the method of fortifier production.

[0037] Figure 2 is a flowchart of an exemplary post-op feeding protocol.

[0038] Figure 3 is a flowchart of the feeding intolerance algorithm.

[0039] Figure 4 is a flowchart of the parenteral nutrition algorithm.

[0040] Figure 5 is a chart of the weaning schedule.

DETAILED DESCRIPTION OF THE INVENTION

[0041] This disclosure features human milk compositions, e.g., a human milk fortifier, human milk fortifier mixed with mother's own milk and standardized ready to feed human milk compositions, as well as methods of making and using such compositions.

[0042] This disclosure also features standardized human milk formulations, which are produced from human milk. Methods of making and using such compositions are also described. These standardized human milk formulations can be used to feed subjects who are undergoing or have undergone surgery, with or without mixing them with other fortifiers or milk, for instance mother's own milk. Human milk formulations can contain various caloric contents, for example, the human milk compositions described herein can provide from about 67 to about 139 kcal/kg/day, for example from about 90 to about 100 kcal/kg/day.

[0043] The compositions of the present disclosure are generated from human donor milk, e.g., pooled milk, which undergoes rigorous genetic screening, processing (e.g., to concentrate nutrients in the fortifier compositions, and/or to reduce bioburden), and pasteurization. The milk can be supplemented with various minerals and/or vitamins.