Lipids for infant formulas

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Abstract – Recommendations for infant formulas (IF) had been established on the basis of human breast milk composition, still considered as “the gold standard”. Historically, till the 20th century, cow milk-based formulas have been used to feed infants when breast feeding was not possible. Later, infant formulas based on cow’s milk proteins but only vegetable oils blends as lipid source became the usual rule in most countries. However, considering “the gold standard”, a lot of changes occurred since the sixties that considerably modified lipid composition of human breast milk which is correlated to the diet of the mothers, who increased their consumption of n-6PUFA to replace saturated fat considered as proatherogenic. This introduced an imbalance in the ratio of linoleic/alpha-linolenic acids (18:2n-6/18:3n-3), limiting the bioconversion to long-chain-n-3 docosahexaenoic acid (DHA, 22:6n-3). Compared to pure vegetable blends and following the usual recommendations for IF, linoleic (LA 15% of total fatty acids), alpha-linolenic acids (ALA 1.5%) and LA/ALA ratio (10), the use of dairy fat blend was beneficial in terms of brain DHA accretion in young rats and a further increase of brain DHA was obtained by using pure dairy fat (LA 2%, ALA 0.8%, LA/ALA 2.3). Cow’s milk presents naturally some similarities (lipid quality, cholesterol, globule structure...) with human breast milk and cannot be compared to pure vegetable blends. Utilization of dairy fat in infant formula should be reconsidered, as well as the absolute amount of polyunsaturated LA and ALA: at least a reduction of LA for IF as well as for lactating women to improve breast milk quality.

Keywords: infant formulas / dairy fat / breast milk / linoleic acid / alpha-linolenic acid

Résumé – Lipides pour les préparations pour nourrissons. Les recommandations pour les formules infantiles ont été établies sur la base de la composition lipidique du lait maternel, considéré comme le « gold standard ». Historiquement, jusqu’au milieu du 20e siècle, le lait de vache a été utilisé pour le nourrisson quand l’allaitement maternel n’était pas possible. Depuis plus de 50 ans, les formules infantiles sont préparées sur une base de protéines laitières mais à partir de mélanges d’huiles purement végétales qui miment la composition du lait maternel. Depuis les années 1960, la composition lipidique du lait maternel a évolué, suite aux modifications du régime des mères qui ont remplacé les acides gras saturés déclarés pro-athérogènes, par des acides gras polyinsaturés n-6 qui ont induit un déséquilibre du rapport n-6/n-3 réduisant potentiellement la bioconversion en longues chaînes n-3 (acide docosahexaénoïque DHA). La ré-introduction des lipides du lait de vache, comparée aux formules purement végétales et selon les recommandations pour formules infantiles, induit une augmentation des niveaux de DHA du cerveau de jeunes rats, et l’utilisation de lipides laitiers purs (baisse des apports en polyinsaturés : LA 2% vs. 15% et ALA 0,8%) améliore encore l’accumulation du DHA dans le cerveau du jeune rat. Le lait de vache présente naturellement des similarités (qualité des lipides, cholestérol, structure des globules lipidiques...) avec le lait humain qui ne peuvent être comparées aux formules purement végétales. En conséquences, l’utilisation de matières grasses laitières devrait être reconsiderée dans la préparation des formules infantiles tout comme
1 Introduction

Lipids are essential in early life for human brain and vision development: among lipids, n-3PUFA and specifically docosahexaenoic acid (DHA, 22:6n-3) accumulate in human brain essentially from 30 wk of gestation to 5 years-old children. DHA could represent 25% of total FA in some brain structures and 50% of total FA of the retina.

N-3PUFA deficiencies during gestation and/or lactation could have dramatic impacts later on cognitive and mental diseases, or metabolic diseases such as obesity or metabolic syndrome (printing) in adults (Alessandri et al., 2004; Ailhaud et al., 2006).

N-3 and brain in early life: from dietary ALA? or DHA?

Foetal and neonate brain DHA content is influenced by the variations in maternal n-3PUFA dietary intake during pregnancy and lactation (Guesnet et al., 2018). It has been demonstrated in the rat that the DHA status during the foetal period or in the young is not different if the mother is fed with the n-3PUFA precursor (alpha-linolenic acid, ALA: 18:3n-3) or with the preformed long-chain-n-3 (LCn-3): DHA via fish oil rich diet (Childs et al., 2011).

Breast milk contains very low levels of DHA and arachidonic acid (ARA, 20:4n-6) (0.1–1% and 0.4–0.9%, respectively) and some formulas contain added preformed LCn-6 and LCn-3 (ARA and DHA). However, after delivery, if DHA could be provided as preformed, it has been shown that an adequate intake of n-3 precursor (ALA) is able to cover the needs for the human adult brain DHA, via a proper liver conversion to LCn-3: 3.8 mg/brain/day for humans (Rapoport et al., 2007; Domenichelli et al., 2015).

The addition of DHA to infant formula has not been consistently shown to have benefits in visual, neural or growth outcomes (Campoy et al., 2012; Makrides et al., 2009), but a benefit could be obtained with supplementation of lactating women with DHA on psychomotor and attention of children later during childhood (Jensen et al., 2010). Addition of preformed ARA remains controversial and no obligation of supplementation was retained by EU (EFSA, 2014), while DHA supplementation during the last trimester of gestation in human and during lactation has been proposed and supplementation of infant formulas with DHA will be the rules in 2020 as imposed by EU (EFSA, 2014).

The recommendations for infant formulas has always been established on the basis of human breast milk composition and is still considered as the “gold standard”. However, some changes occurred since 60 years by the increase of n-6 intake of mothers inducing an imbalance in the breast milk n-6/n-3 ratio which have shown some defavorable effect on LCn-3 which are necessary for the early development, particularly for the brain and also for health later in life (Ailhaud et al., 2006; Rolland-Cachera, 2018). Dairy fat which was usually used to replace breast feeding could be a healthy alternative to pure vegetable formulas to regulate this excess of n-6 and to optimize the infant formula lipid quality.

2 History of infant formula: evolution of cow’s milk utilization

Till the 20th century, cow’s milk had been used to feed infant when breast feeding was not possible, and later, infant formulas based on vegetable oil blends became the usual rule and mimic quite well the lipids of human milk.

Evolution of cow’s milk utilization (Barness, 1987; Stevens et al., 2009)

Since 2000 BC, milk from animals (cow, sheep, goat, donkey, camel...) has been used for human babies when necessary. Formulas containing dairy fats were used till the middle of the 20th century, and continue to be used in a few countries.

Historically, in 1784, dairy fat has been recognized as an alternative to breast milk. The sterilization introduced by Nicholas Appert in 1810, associated to the apparition of glass flasks, helps to the development of cow’s milk artificial feeding, as well as the use of cow’s milk to solubilize food powder for babies introduced by Von Liebig (around 1867). Then, all over the world, companies developed this process (Nestlé 1867, Picot 1896, Guigoz 1908, Mead Johnson 1911…) till 1927, when the first formula from pure vegetable source was proposed and maintained till nowadays.

Evolution of Formula reglementations during the 20th century indicated a progressive reduction of the proportions of cow’s milk to be introduced in the formula, associated to a switch for specific needs of essential fatty acids. Till 1976, more than 60% of dairy fat in infant formula was still the rule; then in 1978 a reduction to 50% of dairy fat was proposed associated to a proper level of linoleic acid (LA;18:2n-6) since its essentiality has been proven. Finally in 1994 all the previous rules have been rejected to propose in 1998 the definition of a minimum content of LA and of an LA/ALA ratio between 5–15.

Interestingly in 2008: long-chain n-6 and -n3 were only “authorised”: arachidonic acid (ARA, 20:4n-6) the most important derivatives of LA precursor of n-6 family should represent 1% of total FA and should be more represented than the derivatives from ALA precursor of the n-3 family: EPA (eicosapentaenoic acid 20:5n-3) and DHA (docosahexaenoic acid 22:6n-3); and the following conditions had to be respected: ARA > DHA > EPA.

However, in the seventies, a come back to the promotion of breast feeding is observed and systematically proposed to women at delivery.

More recently, reglementation from EU (EFSA, 2014) stipulates that the levels of LA and ALA should cover a ratio

Mots clés : formules infantiles / lipides laitiers / lait maternel / acide linoléique / acide alpha-linoléïque
between 5 to 15 despite the fact that for adults the tendency is to reduce this ratio as low as possible (5–6). An obligation of DHA supplementation but not for ARA will be the rules in 2020 as imposed by EU (EFSA, 2014)

3 Breast feeding: the gold standard

3.1 The recommendations for infant formulas had always been established on the basis of human breast milk composition and is still considered as the “gold standard”

The content of lipids in human milk is variable geographically and during lactation (3–4 g/100 g) and is mostly represented as triglycerides (95%). It contains 34–47% of saturated fatty acids (palmitic acid: 17–25% of total fatty acids), about 31–43% mono-unsaturated fatty acids (oleic acid: 26–36%) and about 12–26% n-6PUFA and about 0.8–3.6% n-3 PUFA (Delplanque et al., 2015). The essentiality of LA and ALA were recognized since the first observations of deficiency (Holman et al., 1982; Bourre et al., 1989, 1990) and ALA represents a precursor of LCn-3 (DHA) needed for a proper development of brain of infant. LA and ALA should be provided in proper quantities and proportions (LA/ALA ratio), but these definitions have been often modulated over the last years.

The essential PUFAs LA and ALA content in breast milk depend on the mother’s diet and thus vary widely between countries (respectively from 10 to 24% of fatty acids and from 0.6 to 1.9% of fatty acids) (Delplanque et al., 2015). Furthermore, the most important changes occurred in the sixties, that considerably modified the lipid composition of human breast milk depending of the mother diet, who, similarly to all western populations, increased their consumption of n-6PUFA (LA) to replace saturated fat, considered at this time, to be pro-atherogenic for adults.

Evolution of breast milk composition (Fig. 1) has been studied and reported by Ailhaud et al. (2006): in US as an example since 1940 an increase of LA from 5% to more than 16% in 2000 has been observed. At this time, the levels of ALA (n-3) were not clearly identified, but it has been established that the levels of ALA remained more or less stable from the seventies to 2000. Consequently, the LA/ALA ratio increased from about 6 to more than 16 in 2000 depending of populations (Ailhaud et al., 2006), limiting potentially the bioconversion to LCn-3 (i.e. DHA) (Uauy et al., 1990; Guesnet et al., 2011), which are of major importance for the brain development in the young and against numerous disease in young, adult and elderly. These observations have been found again in several other countries such as Great Britain, but variations were less marked than in US (Ailhaud et al., 2006).

Taking in account the recent dietary recommendations to reduce this LA/ALA ratio for the general population, the increase observed in breast milk is just against the mainstream, and considering the last 50 years evolution of breast milk composition we should be cautious about the definition of a “gold standard” in terms of n-6 and n-3 PUFA.

These recent modifications in human breast milk (reflecting mother’s dietary changes) induced probably the most important changes in the baby diet since many centuries or ever seen in the animal phylogeny, since all mammals show more or less comparable milk FA composition (at least for some lipids or FA) and as mentioned previously, it has been reported that a relationship could be established with some metabolic diseases observed in adulthood (Clark et al., 1992; Ailhaud and Guesnet, 2004; Ailhaud et al., 2008; Pedersen et al., 2012).

However, some “positive” changes could be expected and has been reported after 2000: the recommendations to reduce the LA/ALA ratio for the general population was also applicable to the lactating women with a reduction of dietary intake of LA associated to an increase of ALA, at least in France (Boué-Vaysse et al., 2009).

3.2 Reduction of omega6 intake recommended for adults, what about babies?

The increase consumption of n-6PUFA is now controversial for adults in terms of cardio-vascular protection as well as the saturated fat reduction which has been considered as the bad guy for the last 60 years. The “Seven Countries Study” (Mariotti et al., 1982) who initiated the changes to profit to dietary PUFAs has been revisited and it has been shown that finally (Ramsden et al., 2013) only PUFA-3 were positively associated to a cardio protection (antiaggregant, limiting the infarct clot formation) while n-6 were not active, even worse, being pro-inflammatory and so promoting cardiovascular risk when in excessive amount in the diet. However, LA as a n-6PUFA is still an “essential FA” which means that a minimum intake is necessary to avoid deficiency for reproduction or atopic diseases. It is now proven that there is no need of an excess of n-6PUFA if a proper level of n-3PUFA is associated to the diet: “These results point out the actual overestimation of the physiological LA requirement also questionable in human, and the importance to consider the presence of dietary ALA to set up recommendation, for LA and thus avoid LA
excess since the literature also points out its deleterious effects”... (Guesnet et al., 2011; Choque et al., 2015)

3.3 There are some well-evidenced negative effects of n-6PUFA excess

High LA intake inhibits omega3 synthesis in humans and DHA incorporation in tissues (Gibson et al., 2013). High LA as well as high arachidonic acid inhibit omega3 synthesis in humans and promote cardiovascular diseases via an increase level of inflammation.

High n-6PUFA associated with a high LA/ALA ratio, promote development of adiposity (Ailhaud et al., 2006; Vidakovic et al., 2016; Rolland-Cachera, 2018)

Another quite recent demonstration of deleterious effects of high LA level is shown in the Eden Study, showing that even a high LA in thecolostrum could limit the benefit of colostrum DHA on cognition in children (Bernard et al., 2017).

As mentioned above, n-6PUFA intake is essential for infant formula, but Cuthbertson in 1976 pointed out the high levels of n-6PUFA in the first preparation of pure vegetable formula and already proposed to reduce it to levels equivalent of dairy fat (Cuthbertson, 1976).

So, intake of LA levels could be reduced with a concomitant omega3 increase: 1% LA intake and ratio of 2 for LA/ALA should be enough to maintain a proper equilibrium for an optimal bioconversion to LCn-3 (Guesnet et al., 2011; Choque et al., 2015)

3.4 Could we improve breast milk and infant formula by a reduction of n-6PUFA?

For breast milk there is a need to modify mother diet: an excess of LA dietary intake by mothers (during gestation and lactation) will take time to be modified (reduced).

For infant formula: theoretically, it should not be necessary to wait the dietary modification of Human population for an optimization of infant formula and to reduce LA values, now. But EU should approve or propose these modifications...

Infant formulas blended with dairy fat, with naturally low LA levels (2%), could be the solution to reduce the LA level and to improve the LA/ALA ratio for a better bioconversion to DHA.

Some studies in human (Sanders and Naismith, 1979; Courage et al., 1999; Gianni et al., 2018) or animals (Du et al., 2012, Delplanque et al., 2011, 2013; Oosting et al., 2015) already showed the benefit of pure or blended formulas with dairy fat.

Infant formulas could be easily improved with dairy fat or dairy fat blends.

4 Infant formulas based on vegetable oils or dairy fat (Tab. 1a and 1b)

If infant formulas, based on blends of vegetable oils, mimic quite well the 20th century human breast milk composition in terms of the more represented FA and of essential FA, they missed for example: cholesterol, some short/medium chains fatty acids and the proper sn2-position of palmitic acid on triglycerides; however some of these components could be provided by addition of specific oils or products (ex.: coconut for short/medium chains, etc). Furthermore, the size and structure of globules are quite different from mammal globules inducing different metabolismation (Bourlieu et al., 2017; Le Huërou-Luron et al., 2018).

From this point of view, cow’s milk fat presents naturally much less differences with human breast milk than vegetable blends: a better representation of sn2-position of palmitic acid, similar content of cholesterol and of short and medium chains (C6:0 to C12:0). All these FA present specific functions (Delplanque et al., 2015): for example the presence of short/medium chains could help to limit the oxidation of PUFA precursors and so, could increase the bioconversion to LCPUFA (Lehner et al., 2006), the presence of myristic acid is important for acylation of proteins (Rioux et al., 2011). Furthermore, some fatty acids whose concentration are quite confidential (ex.: nervonic acid) could be of interest during the early brain development (Jamieson et al., 1999) and are present in breast and cow’s milk while totally absent in vegetable formulas.

However, the most striking difference between breast milk and cow’s milk is the content of LA around 10 times less (1.5% vs. 10–24%, respectively), while ALA is quite similar (0.4–0.8% vs. 0.7–2%), inducing drastic differences in terms of LA/ALA ratio from 10 to less than 3. These differences could be attributed to the changes in human mother’s diet, enriched in n-6PUFA since more than 50 years (see above).

To follow the existing rules based on breast milk composition, all infant formulas prepared from manufacturers are made of blends of vegetable oils containing LA and ALA (12–15% and 1.5 to 2.5%, respectively), with an LA/ALA ratio which vary from 5 to 15.

Improvement of LC-PUFA status and brain DHA content with dietary formulas containing dairy fat in human and animal model

Studies in infants showed that dairy fat formula could improve the levels of DHA in their red blood cells compared to pure vegetable formulas and the DHA values were closer to those obtained with breast feeding (Sanders and Naismith, 1979; Courage et al., 1998; Gianni et al., 2018)

Studies in animal model

In an attempt to validate the re-introduction of cow’s milk fat in infant formula, we recently studied the impact on blood and brain DHA levels of young rats, of dairy fat included in different blends of vegetable oils complying with the lipids recommendations for infant formulas (LA: 16%; ALA: 1.6–2.5%; LA/ALA ratio: 10-5) (Delplanque et al., 2011, 2013; Du et al., 2012). We also evaluated the impact of pure dairy fat presenting very low levels of LA and ALA (1.9% and 0.8%, respectively), but with a proper LA/ALA ratio (2.6) which we compared to previous ones and to rapeseed oil rich in ALA (8%). We focused on the evaluation of the DHA level of brain which is an important goal in neonates. Rat is a proper animal model for these nutritional studies and has been used to establish recommendations for infant nutrition since many years (Bourre et al., 1989, 1990).

The three main findings of our studies are:
– dairy-fat-based diet (50% dairy, 50% vegetable oils) with 1.5% ALA content is more efficient than a pure vegetable oil blend with as much ALA (1.5%) and the same LA/ALA
Specific and complex component of dairy fat could be an explanation, such as the short/medium-chain fatty acids which are highly oxidizable after absorption (Rolland et al., 2002; Bendixen et al., 2002) and may thereby spare ALA from oxidation (Jones, 1994), and favor ALA partitioning towards the desaturation and elongation pathways, increasing the LCn-3 (DHA) levels (Du et al., 2012);

dairy-fat-based diet (50% dairy, 50% vegetable oils) enriched with 2.3% ALA is even more efficient (Du et al., 2012). This could be attributed to both the increased level of dietary ALA and the concomitant decrease in the LA/ALA ratio (from 10 to 5) which has been recognized as an important factor driving the bioconversion of ALA into DHA, because of the competition between the parent n-3 and n-6 fatty acids for desaturation and elongation pathways (Gibson et al., 2013);

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Table 1a. Fatty acid composition of human milk, cow’s milk and infant formulas (% of total fatty acids). Saturated and mono-unsaturated fat in human milk, dairy fat and vegetable or dairy/vegetable blends of infant formulas. Short / medium chains FA (SMC) are missing in vegetable formulas (gray cells for absence of FA or non detectable values), but could be replaced by SMC from coco oil. Adapted from Delplanque et al. (2015).

<table>
<thead>
<tr>
<th>Saturated</th>
<th>Breast milk</th>
<th>Dairy fat</th>
<th>Blend of dairy and vegetable oil</th>
<th>Vegetable formula (palm)</th>
<th>Vegetable formula + coco oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyric acid</td>
<td>C4:0</td>
<td>ND</td>
<td>2.6</td>
<td>0.6–0.7</td>
<td>ND</td>
</tr>
<tr>
<td>Caproic acid</td>
<td>C6:0</td>
<td>0.03–0.79</td>
<td>1.9</td>
<td>0.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Caprylic acid</td>
<td>C8:0</td>
<td>0.08–0.61</td>
<td>1.2</td>
<td>0.4</td>
<td>1.0–1.5</td>
</tr>
<tr>
<td>Capric acid</td>
<td>C10:0</td>
<td>0.72–1.71</td>
<td>2.9</td>
<td>1.1–1.2</td>
<td>0.9–1.3</td>
</tr>
<tr>
<td>Lauric acid</td>
<td>C12:0</td>
<td>2.31–6.74</td>
<td>3.5</td>
<td>1.3–1.6</td>
<td>7.8–11.5</td>
</tr>
<tr>
<td>Myristic acid</td>
<td>C14:0</td>
<td>3.98–8.67</td>
<td>10</td>
<td>5.0–5.5</td>
<td>4.0–5.5</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td>C16:0</td>
<td>16.6–25</td>
<td>26–32</td>
<td>16.5–20.4</td>
<td>26.1–29.5</td>
</tr>
<tr>
<td>Stearic acid</td>
<td>C18:0</td>
<td>3.39–6.89</td>
<td>10</td>
<td>5.4–6.1</td>
<td>3.3–4.1</td>
</tr>
</tbody>
</table>

Table 1b. Fatty acid composition of human milk, cow’s milk and infant formulas (% of total fatty acids). N-6 and n-3 PUFAS in human milk, dairy fat and vegetable or dairy/vegetable blends of infant formulas. ALL LCn-3 and LCn-6 are missing in vegetable formulas (gray cells for absence of FA or non detectable values), but could be replaced solely by preformed ARA and DHA. Please note that in dairy fat 18:2n-6 (LA) is very low (underlined), almost 10 times less than in breast milk while 18:3n-3 (ALA) is within the range of human breast milk, inducing the lowest (best) LA/ALA ratio. Adapted from Delplanque et al. (2015).

<table>
<thead>
<tr>
<th>n-6 PUFA</th>
<th>Breast milk</th>
<th>Dairy fat</th>
<th>Blend of dairy and vegetable oil</th>
<th>Vegetable formula (palm)</th>
<th>Vegetable formula + coco oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic acid</td>
<td>C18:2 n-6</td>
<td>10.1–24.3</td>
<td>1.8</td>
<td>15.6–16.3</td>
<td>16.8–17.8</td>
</tr>
<tr>
<td>Gamma-linolenic acid</td>
<td>C18:3 n-6</td>
<td>0.06–0.23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>C20:4 n-6</td>
<td>0.45–0.86</td>
<td>0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenic acid</td>
<td>C22:4 n-6</td>
<td>0.04–0.47</td>
<td>0.01</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>n-3 PUFA</th>
<th>Breast milk</th>
<th>Dairy fat</th>
<th>Blend of dairy and vegetable oil</th>
<th>Vegetable formula (palm)</th>
<th>Vegetable formula + coco oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-linolenic acid</td>
<td>C18:3 n-3</td>
<td>0.67–1.9</td>
<td>0.4–0.8</td>
<td>2.4–2.5</td>
<td>1.9–3.4</td>
</tr>
<tr>
<td>Steardonic acid</td>
<td>C18:4 n-3</td>
<td>0.23–0.68</td>
<td>0.12–0.16</td>
<td>0.04–0.08</td>
<td></td>
</tr>
<tr>
<td>Eicosatrienoic acid</td>
<td>C20:3 n-3</td>
<td>0.05–0.4</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eicosapentaenoic acid</td>
<td>C20:5 n-3</td>
<td>0.06–0.33</td>
<td>0.05–0.08</td>
<td>ND</td>
<td>0.1</td>
</tr>
<tr>
<td>Docosapentaenoic acid</td>
<td>C22:5 n-3</td>
<td>0.16–0.54</td>
<td>0.09–0.12</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Docosahexaenoic acid</td>
<td>C22:6 n-3</td>
<td>0.09–1.03</td>
<td>0.01</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Ratio LA/ALA</th>
<th>Blend of dairy and vegetable oil</th>
<th>Vegetable formula (palm)</th>
<th>Vegetable formula + coco oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.45–11.9</td>
<td>2.3–3.5</td>
<td>6.2–6.7</td>
<td>4.9–9.4</td>
</tr>
</tbody>
</table>

- added DHA 0.2–0.3
- added DHA 0.2–0.3
- added ARA 0.1–0.6
- added ARA 0.1–0.6
dairy-fat-based diet containing pure dairy fat (100%) with only 0.8% of ALA and 1.9% of LA is as efficient as an 8% ALA rapeseed diet (22% LA) to increase the brain DHA in the growing rat, both presenting a similar very low LA/ALA (less than 3) and present results comparable to the 2.3% ALA dairy/vegetable blend.

The role of Delta6-desaturase could be involved in this process and is crucial to explain these last results: ALA is the precursor of DHA but also its competitor for the last Delta6-desaturase step, and is regulated by substrate levels (Tu et al., 2010). An excess of ALA could represent the first substrate, producing increasing quantities of some LC n-3 (EPA, docosapentaenoic acid: DPAn-3) and secondarily could limit the implication of delta6-desaturase in the second control point for DHA conversion. Explanation for rapeseed is exactly reverse and could represent an excess of precursor, which could limit the bioconversion to DHA, even reducing its level when intake is above the optimal intake (around 2.5–3% of total FA). The proof of this intra-cascade n-3 competition for delta6-desaturase has been validated previously (Morise et al., 2004; Cleland et al., 2005). In our protocol conditions, we observed a stabilization of brain DHA levels with a ratio of 3 to 5 and apparently, there is no real need to increase the absolute amount of n-6 and n-3 precursors to obtain these results: pure dairy fat with only 0.8% of ALA and less than 2% of LA with a ratio around 3 is quite efficient to provide DHA levels required by the brain for neonates and adults (Rapoport et al., 2007; Domenichelli et al., 2015).

Finally, pure dairy fat, despite very low levels of PUFA (1.5–3% LA and 0.5–0.8% ALA) but associated with a very favourable LA/ALA ratio similar to rapeseed oil (maximum 3/1), was able to provide the proper conditions for a bioconversion of ALA to LC n-3 and DHA necessary for the brain of young animals.

Together, these observations clearly demonstrated that brain DHA levels can be substantially improved by dairy fat based-diets. Our data are in good agreements with the results obtained in studies showing that infants fed formulas based on dairy fats (Sanders and Naismith, 1979; Courage et al., 1998) have a higher LC n-3 status than those fed formulas enriched with LA-rich vegetable oils. The use of fats that are low in PUFA such as dairy may confer some metabolic advantages in that they allow better endogenous conversion of ALA to DHA.

5 Conclusions

Recommendations for better n-3PUFA levels during early life is depending on a reduction of 18:2n-6. N-6PUFA needs could be reduced when n-3PUFA are associated in the diet, for infant formulas and for mother diet to correct the breast milk quality.

Furthermore, an excess of 18:2n-6 could limit the accretion of preformed DHA, bioconversion of n-3 ALA to LCn-3 and increase pro-inflammation.

Dairy fat presents the best FA quality for infant formulas: low levels of LA, large similarities with breast milk in terms of variety of FA, cholesterol, sn2 position of palmitic acid on TG, a good representation of “minor” FA comparable to breast milk, presence of medium/short chains and a proper level of ALA and LA/ALA ratio which is presently better than the human breast milk.

Breast milk is still the “gold standard” but should be improved by a reduction of n-6PUFA.

Consequently, the use of dairy fat in infant formula should be reconsidered, as well as the absolute amount of polyunsaturated LA and ALA.

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References


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