



Association between parental self-reported knowledge on soy and phytoestrogen and their children's intake of soy-based infant formulae—a cross-sectional study of Israeli parents

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Abstract

Objectives Though natural phytoestrogen (PE) is a major factor in health authorities' considerations regarding soy-based infant formula (SBIF), missing their concentrations may interfere with parents' informed decision.

Methods We performed an Internet survey investigating soy-related knowledge of parents. We built multiple logistic regression models adjusted for personal covariates for the association between parental knowledge on PE and children intake of SBIF and checked the effect of having children ≤ 2 years old on this association.

Results We enrolled 304 parents, 48.3% men, mean age 33.8 (standard deviation, SD 4.9), mostly with higher education. Of them, 76% had children under two years of age. Mean parental knowledge on PE was 9.83 (SD 3.28) from 20 possible points. Parental knowledge on PE reduced children's intake of SBIF (odds ratio, OR = 0.85 [95% confidence interval 0.70; 1.02]). Stronger inverse association was found for parents with children ≤ 2 comparing with those with older children (OR = 0.85 [0.67; 1.09] and OR = 0.68 [0.39; 1.18], respectively), although these differences were not statistically significant.

Conclusions Adding PE content to information on SBIF may support informed decision.

Keywords Phytoestrogens · Reproductive development and health · Soy-based infant formulae · Parental knowledge · Consumption of soy products

Introduction

Phytoestrogens (PEs), a group of estrogens receptor modulators, are substances of plant origin that are structurally and functionally similar to estrogens (Jargin 2014). Soy-based infant formula (SBIF) contains PE of the isoflavone

class in rather high concentrations. As a result, the plasma isoflavone concentrations in SBIF-fed children are increased up to 11-fold higher compared to those in adults consuming a soy-rich diet (Barnes 1995). SBIF has been used in the USA since 1909, especially for children with cow-milk protein allergies, lactose intolerance and other problems of the gastrointestinal tract (Westmark 2017). Though the concern regarding phytoestrogens was long

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expressed, longitudinal studies were rare (Westmark 2017). After a longitudinal study that did not find differences in growth and development in those fed as infants with cow milk-based formulae compared with SBIF (Strom et al. 2001), the American Academy of Pediatrics concluded in 2008 that SBIF was a safe nutritional equivalent of cow milk-based formulae and recommended SBIF for use in children with lactase deficiency and for children whose parents were seeking a vegetarian-based diet for their infant (Bhatia and Greer 2008). These recommendations have been cited regularly in the pediatric literature related to child nutrition (Kleinman and Greer 2014). Based on this information about SBIF safety, parents who adhere to a vegetarian lifestyle tend to feed their children SBIF even without medical needs. For example, in the study on 1803 mothers of children aged 2–12 months that was performed in Israel it was shown that only for 10.9% of the sample the choice to use SBIF was made based on the child's cow-milk allergy, while in other cases the preference for the use of SBIF had no clinical indications (Berger-Achituv et al. 2005).

However, studies that focused on children's reproductive health suggested that exposure to soy PE has a significant impact on children's later reproductive health (Patisaul and Jefferson 2010). For example, changes in gender-related behavior in girls that had been fed with SBIF were found in the study by Adgent et al. (2011). Another retrospective longitudinal study comparing adults fed in their infancy with SBIF or with cow milk-based formula showed longer menstrual bleeding in women fed with SBIF (Strom et al. 2001). In boys, consumption of soy PE may interfere with the effect of testosterone surge defined as "minipuberty" that occurs during the boy's first few months of life, potentially leading to micro-penis and cryptorchidism (Kurtoglu and Bastug 2014). In a review published in 2010, all four reviewed human studies found differences in sexual development for boys and girls fed with cow milk-based formulae and SBIF (Dinsdale et al. 2011). For example, girls fed with SBIF did not demonstrate a decline in breast tissue during the second year of life, as was found in cow milk- or breast milk-fed children. In boys, low testicular weight was observed for those fed with SBIF in comparison with those fed with breast milk. In contrast, a very recent review (Testa et al. 2018) suggests that the potential harmful effect of SBIF was demonstrated only for children with hypothyroidism, though not excluding the potential harmful effects of PE on child development. All agree that the fact that only rare human studies on the effects of consumption of SBIF were published up to date calls for more investigations on this issue.

Investigations of parental knowledge and beliefs concerning feeding are an important area of early intervention

and prevention, including of possible damage from consumption of SBIF. In this context, Israel is one of the countries that can provide extensive and important information about beliefs and knowledge about soy-based products. Indeed, Israel is one of the world leaders of infant soy products consumption because of Kosher laws restricting milk products being served together with meat/chicken meals. This restriction does not concern soy milk, while soy milk can be used in food together with any other products, making it easier for those practicing a Kosher lifestyle. In addition, last national survey showed increasing tendency to vegetarian lifestyle between Israelis in 2019 comparing to 2010 (Tishner 2014). The extensive consumption of soy-based products enables addressing soy product-related questions in a large population of consumers.

In this study, we aimed to investigate the association between parental knowledge on PE in food products and parents' self-reported intake of SBIF by their children in a population-based sample of participants from different regions of Israel. We hypothesized that parental knowledge on PE is negatively associated with the intake of SBIF in children. We further considered whether having children less than two years of age is a potential modifier of the association between parental updated knowledge on PE and children's intake of SBIF. However, the main assumption is that self-reported knowledge is less than needed for true informed decision, unless product transparent information is presented. Confirming the existence of knowledge–decision association could be a good reason and important step toward requesting the relevant knowledge and promote technologies for reducing their content.

Methods

Study population and instruments

We performed an anonymous Internet-based survey for parents of children less than four years of age. The study was performed in all five regions of Israel (Central, Northern, Southern, Sharon and Jerusalem regions) and included participants from both genders, all ages and socioeconomic statuses. The panel of soy-related questions was developed by the Brandman Institute for research and marketing consultancy. The panel included 13 soy-related questions divided into three major categories: parental knowledge on PE, parental consumption of soy products and children's intake of SBIF. Specifically, the questions assessed parental self-reported knowledge of soy products and possible consequences of PE, temporal/permanent consumption of SBIF by their children, parental permanent/occasional consumption of soy products and their

willingness to obtain additional information on ingredients in different children products. The answers to all questions were of a multiple-choice format.

The socio-demographic information obtained from the survey included gender, age of respondent, income (lower than average, average, higher than average), level of education of parents (primary, secondary and academic education), country of birth, place of living according to the five regions of Israel, marital status, religious status and age of children that was further dichotomized according to the median age of consuming children formulae (≤ 2 years of age; > 2 years of age).

Ethical approval for this study was granted by Brandman Research Institute, being member of the Israeli Ethical Association. Participants did not sign a formal informed consent, as their participation in the Internet-based survey was an indication of free willingness to participate in the study.

Statistical analysis

We transformed the variables obtained as a result of a panel of soy-related questions according to the study hypotheses. Parental knowledge on PE was calculated as a sum of five questions and was used in the analysis as a continuous variable. Children intake of SBIF (question with three categories) and parental consumption of soy products (question with nine categories) were dichotomized for the statistical analysis (yes/no). Descriptive statistics and univariate analysis were performed for all study variables. Because of the relatively small study sample, we considered statistical significance for this study at the $p < 0.10$ level. In that case, we obtained the power of the analysis of 83.0%.

We built multiple logistic regression model on the association between parental knowledge on PE and children's intake of SBIF. Direct acyclic graph, DAG (Textor et al. 2011), was built to visualize possible relationships between study variables and to formulate proper hypotheses (Fig. 1).

The minimal adjustment set according to DAG included age and gender of parents. We added to this main model by stepwise method other socio-demographic variables that showed statistical significance in univariate analysis and additionally built the over-adjusted model adjusted for age and gender of parents, their level of education, having children under two years of age, religious status, marital status, place of living, occupation, income and place of birth. The best model was chosen based on the -2 log likelihood ($-2LL$) and Nagelkerke R^2 . The main adjustment set that we decided to use in this study included the gender, age and education of the parent as a marker of his/her socioeconomic status ($-2LL = 67.8$, Nagelkerke

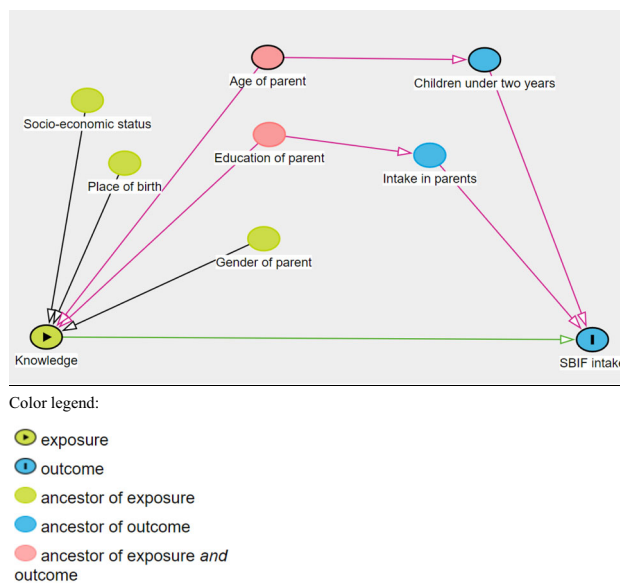


Fig. 1 Direct acyclic graph of possible relationships between study variables

$R^2 = 0.22$). As most of parents (96.0%) used varied amounts of soy products by themselves, we did not include this variable from the multiple regression. Odds ratio (OR) and 95% confidence intervals (CI) were presented for each one of the variables in the model.

Possible effect modification of the main model by having children under two years of age was checked by differences in effect estimates of parental knowledge on PE between those who have and those who do not have children under two years of age. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) statistical software 22.0 version (IBM Corp. Released 2013).

Results

The study sample consisted of 304 participants, with similar rates of men and women, mostly with academic level of education, of whom approximately half live in the center of Israel and are non-religious and married and have children under two years of age. From all parents, 96.0% consumed soy-based products in various amounts/occasions. Most of the children consumed SBIF—permanently or temporally, at least for one month (Table 1). From all parents, 16.6% reported an absolute lack of knowledge on soy PE presence in their children's formulae.

In the univariate analysis, we did not observe any statistically significant relationships between parental knowledge on PE and other socioeconomic parameters: education ($p = 0.81$), income ($p = 0.87$), gender ($p = 0.80$), parental marital status ($p = 0.73$) and religious status ($p = 0.51$), as

Table 1 Description of the study population, Israel, 2016

Variable	<i>N</i> = 304
Male gender of parent, <i>N</i> (%)	146 (48.3)
Age of parents (years), mean \pm SD [min; max]	33.8 \pm 4.9 [24; 44]
Education of parent, <i>N</i> (%)	
Primary	42 (14)
Secondary	68 (22.5)
Academic	193 (63.6)
Place of living, <i>N</i> (%)	
Central region	122 (40.4)
North region	61 (20.2)
South region	58 (19.2)
Sharon region	31 (10.3)
Jerusalem region	30 (9.9)
Non-religious, <i>N</i> (%)	160 (53.0)
Marital status, <i>N</i> (%)	
Married	282 (93.4)
Divorced	6 (2.0)
Income, <i>N</i> (%)	
Lower than average	48 (15.9)
Average	141 (46.7)
Higher than average	84 (27.8)
Have children under two years of age, <i>N</i> (%)	231 (76.5)
Intake of soy-based products (for parents), <i>N</i> (%)	290 (96.0)
Children fed SBIF at least for one month, <i>N</i> (%)	
Overall	242 (80.1)
\leq 2 years old	192 (83.1)
$>$ 2 years old	50 (70.4)
Parental knowledge on PE, mean \pm SD [min, max]	9.83 \pm 3.28 [2; 20]

well as parental consumption of soy products ($p = 0.32$). Although we assumed that religious parents observing Kosher rules are more likely to feed their children with SBIF soy products because it is convenient, we did not observe any relations between religious status of parents and SBIF intake in children ($p = 0.93$).

In fully adjusted logistic regression models, parental knowledge on PE significantly decreased the intake of SBIF in children (OR = 0.85 [95% CI 0.70; 1.02, $p = 0.08$]). Older parents were less likely to feed their children with SBIF, and parents' age was the most prominent factor in this model according to Wald statistics. Education of parents did not affect the SBIF intake (Table 2).

Stronger inverse association was found for parents with children less than two years of age (OR = 0.85 [95% CI 0.67; 1.09]) comparing with those with older children (OR = 0.68 [95% CI 0.39; 1.18]), but confidence intervals of effect estimates in these two layers overlapped (Fig. 2), and the effect modification was non-significant.

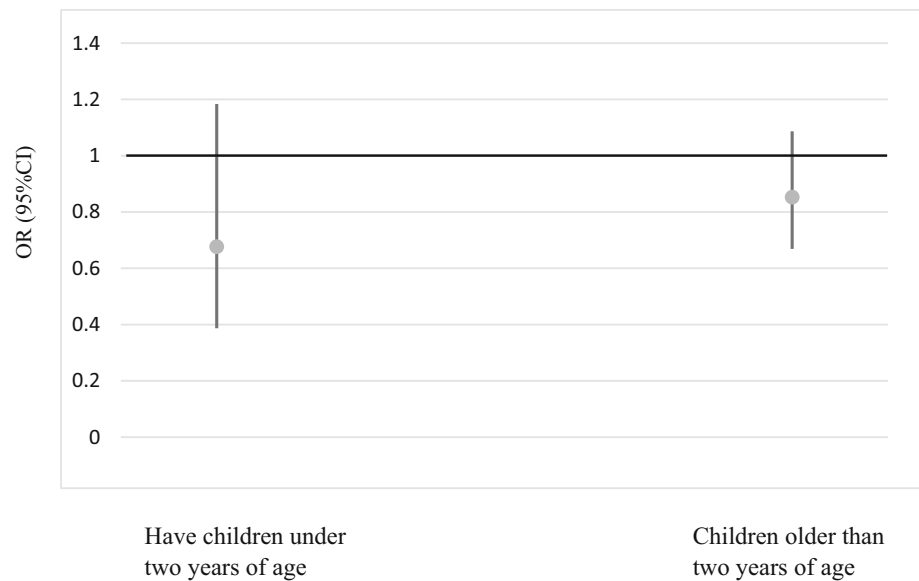
Table 2 Association between parental knowledge on phytoestrogens and intake of soy-based infant formula in children, Israel, 2016

Variable	Main model		
	OR	CI	<i>p</i>
Parental knowledge on PE	0.85	0.70; 1.02	0.08
Gender	4.21	0.83; 21.37	0.08
Age	0.78	0.65; 0.93	0.04
Education	1.68	0.70; 4.04	0.24

Discussion

In this study, we observed that parental knowledge on PE is a significant predictor for their decision of feeding their infants with SBIF. Recently, Amado and Bret (2013a; 2013b) showed that parental perceptions of food are important contributing factors to the child's diet quality. These perceptions are shaped by a complex array of factors that include, among others, cultural and inter-generational

Fig. 2 Effect modification of the association between parental knowledge on phytoestrogens and children intake of soy-based infant formula by having children under two years of age, Israel, 2016



beliefs, social pressure, education, social media and official health communications. The total lack of information provided by manufactures about the presence of PE and its concentrations and medical concerns regarding possible health effects of using these products makes the decision of parents difficult, and they make their decision inconsistent, partly based on their confidence of their physicians and partly without any basis. This situation was clearly demonstrated in an earlier Israeli survey (Berger-Achituv et al. 2005) that found that mothers attempted to use SBIF both because of recommendations of healthcare personnel and despite medical recommendations against SBIF—together suggesting mothers play a greater role than medical personnel in the decision to initiate soy-based formula. Suspected cow-milk protein allergy was responsible for only 10% of all SBIF use in infants, while 90% of the parents used SBIF for non-medical reasons (Berger-Achituv et al. 2005). Even in the case of infants with cow-milk protein allergy, parents frequently select SBIF despite the recommendations by “Nutrition for Healthy Term Infants” of the Canadian Pediatric Society (2005) that recommended use of another kind of children formulae, i.e., the extensively hydrolyzed one (Leung and Otle 2009). Thus, for attaining optimal outcomes and to choose the optimal type of formula, it is critical for parents to obtain firstly transparent contents and targeted product information and medical information about potential consequences of feeding children with SBIF.

Some authors suggest that poor maternal nutrition knowledge is one of the factors contributing to poor dietary intake among children (Duncanson et al. 2013), including that regarding hormone-distracting factors. For example, parents who adhere to a vegetarian lifestyle might not be aware that daily intake of isoflavones in soy infant

formulae is estimated at 1–8 mg/kg body weight/day (Rozman et al. 2006), which is 6 to 11 times higher than the amount consumed by adults on a traditional soy-based Asian diet (Barnes 1995). The study by Cao et al. (2009) showed that urine isoflavones in children fed SBIF were 500 times higher than in children fed cow milk-based formulae. The underestimation of the level of PE in SBIF is related to lack of direct and translational information given by manufacturers, especially facing the fact that the level of PE differs from one product to another within and between brands (Setchell and Cole 2003). For example, in the study by Setchell et al. (1998) the level of isoflavones in five different SBIF differed from 32 to 47 mg/l isoflavones of formula. Another study reports the mean of 65.9 mg/kg of isoflavones in seven different SBIF available in Brazilian market with the huge difference between formulae—from 16.2 till 85.4 mean content of isoflavones (Fonseca et al. 2014). Those studies together demonstrate the inconsistency of concentration and lack of specific information obtained by parents feeding their children with SBIF. Parents would need to compare different products based on labels that provide the information either in mg/l and/or in mg/kg.

Apart from official sources of nutritional information such as health authorities, unfortunately parents may also receive health and nutrition information that is not evidence based and potentially contradictory from informal sources, some of which are profit oriented such as media promotion and commercial Internet sites and retailers, and others—related to personal environmental ethic and beliefs. Anyway, it is impossible for parents to make an informed decision under such circumstances, i.e., missing information with regard to PE content.

Overall, we did not obtain the effect measure modification by age of the child of the association between parental knowledge on PE and children' intake of SBIF. Stronger inverse association was found for parents with children less than two years of age. This finding supports the stronger interests in feeding-related issues for parents of younger children. However, missing the information regarding PE content and biological translation to infant measures can limit parents' interest.

The biological ground for the potential effect of soy PE on reproductive system is rather understandable and is based on the similarity of soy isoflavones to estrogens. Soy isoflavones upon specific circumstances can act as agonists, partial agonists or antagonists to endogenous estrogen through estrogen receptor (Barret 2006). The long-term safety of very high supplemental doses of soy isoflavones, especially for infants, is not yet consistently established. In animal studies, it was clearly shown that PEs have a biological action on male reproductive endocrinology altering body and prostate weight and plasma androgen level in rats (Weber et al. 2001). Another study on male rats showed the impaired mating and fertility and low sperm volume in rats fed with PE in comparison with the control group (Atanassova et al. 2000). Male monkeys fed soy-based formula during 45 days in amounts similar to that reported in 4 months human infant fed on 100% SBIF, exhibited 53–70% lower mean levels of testosterone than their twins fed with cow milk, where the dose–response relationships are shown between the intake of soy product in gram and testosterone level reduction (Sharpe et al. 2002). Female rats fed with soy milk showed advanced mean day of vaginal opening and decreased progesterone level in mature rats (Lewis et al. 2003). In mice, early exposure to PE leads to delayed parturition, decreased fertility and altered estrous cycling (Jefferson et al. 2009). Human studies on the effect of PE on reproductive system of children are insufficient and mostly cross-sectional and therefore do not provide long-term information on the effects of PE on children's affected responses.

Limitations of the study

This study has several limitations. First, we had a relatively small sample size for the study investigated knowledge. Although a power of analysis with such sample size was 83% while reducing the significance level to 10%, larger sample size might be necessary to analyze such a complex concept.

Another limitation of this study was the method of investigating parental use of soy products. We did not obtain information on the parents' lifestyle, for example are they vegetarians or vegans or do they use soy products as a supply product in non-bordered diet. In fact, we

analyzed the attitude of parents toward soy-based products and not their actual lifestyle, as the main focus of this study was SBIF. Nevertheless, the finding concerning the absence of an interaction between parental use of soy products and their knowledge on PE seems to be interesting and deserves additional/further investigations.

Strengths of the study

This is a population-based study with participants from all regions of Israel that can represent the whole Israeli population. We included in our analysis parents living in different regions of Israel, with different educational, marital, economic status, with the similar rates of religious and non-religious individuals. This gave us the opportunity to form conclusions on the overall population of Israel. We strongly believe that the conclusions formulated in this study may shed light on patterns existing in other communities beside Israel and potentially suggest their use as a basis for formulating/developing food information policies in other countries.

Conclusions

As children fed with SBIF are exposed to high levels of PE in early life, at the period that is critical for their reproductive and brain development, the use of SBIF has to be based on weighted and informed decision of parents. For this purpose, it is essential to provide maximum information about these products, including innate bioactive components. Parents should have a maximal accessible information on possible consequences of different infants' formulae's components, including hormone-distracting factors.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval Ethical approval for this study was granted by Brandaman research institute, being member of the Israeli Ethical Association. Participation in the Internet-based survey was an indication of free willingness to participate in the study.

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