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Contribution of food additives to worldwide variations in the prevalence of childhood asthma symptoms

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Abstract:

Objective To examine the association between food additive consumption and international asthma prevalences as measured in Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC) study.

Design Examination of data from government food analyses, independent food analyses, trade and agriculture reports and histories.

Setting 14 countries representing 74 ISAAC centres with diverse asthma prevalences.

Population 13-14 year-old children.

Main outcome measures Total food additive intake estimated as the density of McDonald's fast food outlets per million population (McScore); estimation of the consumption of sulphite preservatives in meat; data on current wheeze as a measure of asthma prevalence from the 1996 ISAAC written questionnaire.

Results A highly significant positive correlation ($r=0.94$, $p<0.0001$) was found between estimated food additive intake and ISAAC asthma rates by country. 20-30% of asthmatic children could be sensitive to sulphites according to a recently updated estimate by the World Health Organisation. Major sulphite vectors for children are drinks, sulphited meat, hot chips (French fries) and, especially for young children, dried fruit. Sulphite vectors except meat are associated with the Western supermarket diet; sulphite as a meat preservative is used only by English and Spanish-speaking countries.

Conclusions Food additive consumption can explain the increase in asthma symptoms associated with the Western lifestyle; international variations in childhood asthma prevalence including high rates in English-speaking and Spanish-speaking South American and lower rates in European and developing countries; higher asthma rates in preschoolers; and a decline in childhood asthma in some countries.

Keywords: asthma, children, prevalence, sulphites, food additives

Introduction:

Worldwide reports indicate an increase in the prevalence of childhood asthma[1 2], with large variations between countries[3] and recent declines in the UK[4], Italy[5], Australia[6], Hong Kong[7] and Singapore[8].

To date there is no unifying hypothesis to explain these patterns. They cannot be accounted for by recognised environmental factors such as air pollution[9 10] or house dust mite allergens[10 11]. The hypothesised protective effects of poor hygiene, family size and overcrowding have not been supported by recent data from Latin America[9] and rural Xhosa children in Africa[12]. Recent findings suggest that certain components of Westernised foods may contribute to variations in asthma prevalence and a protective role of dietary antioxidants has been proposed[13-15] although results of studies have been inconsistent[16].

Food additives and especially sulphite preservatives in both foods and medications have been associated with asthma exacerbation in many countries over many years[17-25] and asthmatics have been shown to improve on additive-free diets[26-28]. However, the effects of food additives on children may have been underestimated. With the realisation that children eat and drink significantly more than adults proportional to their body weight and consequently take in more food additives, the World Health Organisation (WHO) revised upward their estimate of prevalence of sulphite sensitivity from 4% of the asthmatic population to 20-30% of asthmatic children[29]. Nevertheless, degrees of sulphite sensitivity that may contribute to sub-clinical respiratory tract inflammation were undetected by current test methods[25]. Likewise, standard challenge testing of food additives was found to miss the majority of additive responders unless preceded by a comprehensive food chemical elimination diet[28]. In the only study of asthmatic children ever to use such an elimination diet, 66% reacted to sulphite challenge[17].

The main sulphite vectors for children are drinks[23 30-33], sulphited meats such as sausages[30 34-42] and potato products such as hot chips (French fries)[32 34 37 43-46] due to the levels of sulphites used in these foods (table 1) and frequency of consumption. For those who eat them, dried fruit can be the greatest sulphite vector[32 34 37 42 45] especially for young children, with Australian 2-year-olds consuming 70 times more dried fruit than 12-year-olds (21.5 compared to 0.3 grams/day)[40].

Smaller amounts of sulphites from a wide variety of processed foods can contribute to total intake, including bread and margarine[40], jams, jellies, toppings, dried vegetables, packet

soups, baked goods and common processed food components including lemon juice, vinegar, beet sugar, corn syrup, glucose syrup, cornstarch and potato starch[46 47] as well as crustacea[32 41 44] and medications[48].

The Acceptable Daily Intake (ADI) of sulphites is 0.7 mg per kg of bodyweight, although asthmatics can be affected by lower levels of sulphites[25 46]. Apart from sulphites in Spanish meat[35 38], English-speaking countries generally reported the highest use and intake of additives[29 31 36 37 40 42]. Japan reported the lowest intake of sulphites, with an average daily intake per person of 5% of the ADI[29] compared with 68-128% of the ADI found in an independent study in the UK based on detailed dietary records combined with actual sulphite analyses[37].

Additives other than sulphites that are common in processed foods and drinks and have been associated with asthma include artificial colours[19 25 28 49], benzoate preservatives[19 27] and the antioxidants butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT)[50], also known to cause pulmonary inflammation in rodents[51] .

To test the hypothesis that consumption of certain food additives can explain variations in childhood asthma prevalence, the association between estimated food additive consumption and international asthma prevalences in 13-14 year-old children as measured in Phase One of the ISAAC study was examined.

Methods:

Additive regulations and consumption vary considerably between countries. Sulphites in particular present unique problems when calculating intakes because, unlike most additives, they can be destroyed by storage or heat[29], although sulphites in meat are reduced only up to 50% during cooking[37 38]. Higher levels are used during warmer weather[34] and in the absence of refrigeration[36]. A combination of consumption data with residue levels determined by analysis is required[32 37] but is rarely available. Since there was insufficient comparable data to calculate actual food additive intake[32-40 43 47 52] in ISAAC countries, proxy measures were necessary.

Fast food outlets have accompanied the rise in supermarket food retailing since the 1960s and are paralleled by the increase in the processed potato industry[53 54]. As the largest fast food operator in the world, every day the McDonald's corporation serves approximately 46 million people in 30,000 outlets in 120 countries. The density of McDonald's outlets was used as the proxy measure of exposure to additives in processed foods and drinks, calculated by dividing the number of outlets per country by the population of that country in millions (McScore). McDonald’s 2001 statistics were closest to the ISAAC data collection date[54]. For China and South Africa, both large countries with uneven development, McScore was calculated for the ISAAC centres of Guangzhou[55] and Capetown[56].

Countries were included where there was at least one McDonald's outlet as well as information about the use of sulphites and other food additives. Information about Australia and New Zealand was aggregated as they have the same food regulations[41], similar food intake[57], McScore (37.4, 38.9) and asthma prevalences (29.4%, 30.2%). Information about food additives was collected through Medline searches, WHO additive intake evaluations, government and independent surveys and 'grey literature' such as trade reports, as referenced herein.

Product	mg sulphite		Sulphite survey*				MPL†
	per (serving)		mean	range	number	country	
Dried apricots	56	(50g)	1125	765-2910	10[34]	England	2000
Sausages cooked	52	(100g)	518	-	1[37]	England	450
Sausages cooked	23	(100g)	227	100-450	24[40]	Australia	500
French fries frozen	7	(200g)	34	19-149	50[34]	England	100
Dried mashed potato	5	(30g)	171	154-189	2[37]	England	400
Fruit drink concentrate	5	(200ml)‡	123	4-268	65[31]	England	250
Beef mince cooked	4	(100g)	44	0-890	32[40]	Australia	0
Beef mince raw	na		23	0-4100	1352[36]	Scotland	0
Hamburgers raw§	na		216	-460	15[34]	England	450
Hamburgers raw	na		-	136-266	6[39]	Spain	450
Hamburgers raw	na		1430	188-7565	40[35]	Spain‖	

Table 1 Main surveyed sulphite vectors for children

* Sulphite mean and range in mg/kg, number of samples and country reporting. † Maximum Permitted Level of sulphite in product in mg/kg at time and place of survey. ‡ Diluted according to instructions. § Hamburgers consist of minced meat with a minimum cereal content, unlike McDonald's meat patties. ‖ In Spain prior to 1995 there were no limits on sulphites in hamburgers.

Meat is one of the most important sulphite vectors for children[30 34 35] (table 1). However, sulphited meats are not used in some countries, so as well as a McScore for processed foods, a country-by-country score was needed to indicate the use of sulphites in meat. English and Spanish speaking countries have been the main consumers of sulphited meats[35] since South American[58] and Australian[59] beef producers pioneered the use of sulphites as meat preservatives in the pre-refrigeration era. High levels of sulphites[34 36 40] in English-style breakfast sausages and other forms of sulphited meats are consumed frequently[40 60] by children in the UK and Australia/NZ (table 1) whereas consumption of sulphited meat may be moderate in the former British colony of Capetown[61] with a mixed heritage population. In Spain, some extremely high levels of sulphite use[38] were reduced[35 39] to comply with EU legislation[62] (table1). When combined with possible less frequent consumption[63 64] than English children, this resulted in a moderate rating for Spain. In the absence of data, we assumed sulphite levels in South American countries were similar to the high Spanish levels before EU harmonisation. Other countries all have a low use of sulphited meat: the USA prohibited all use of sulphites in meat in 1959[44]; in European countries other than the UK and Spain, sulphites are permitted in meat but are generally not used[32 35]; East Asian countries have a tradition of low consumption[57] of fresh unsulphited meat from wetmarkets[54] and India is predominantly vegetarian.

The mean sulphited meat score was weighted to match the mean McScore, since one serve of highly sulphited meat per week can be the equivalent of a daily glass of fruit drink or multiple serves per day of low doses of sulphites in numerous processed foods[38].

Results:

Table 2 shows the estimated consumption of asthma-associated additives including sulphites in processed foods and sulphites in meat for children in 14 ISAAC countries covering 74 of the 155 centres in the original ISAAC study. There was a highly significant positive correlation ($r=0.94$, $p<0.0001$) between the total additive score and the prevalence of asthma according to phase one of the ISAAC study.

There were wide variations in estimated sulphite consumption. A village child on a subsistence diet would ingest no sulphites per day compared to a high sulphite consuming child in Italy on 23 mg per day[32] and it would be possible for a preschooler in Australia to consume 112 mg of sulphites by eating 2 serves of dried apricots per day (table 1).

Per kg body weight, on average Australian two-year-olds consumed approximately twice as many sulphites as 12-year-olds, not including sulphited drinks that are a major sulphite vector for children. In developed countries, the density of fast food outlets was found to be higher in low income areas[65] and frequency of fast food restaurant use was associated with greater body weight[66]. Sulphite use was greater at higher temperatures[34 36], and in the absence of refrigeration[36].

Country or city	McScore	Sulphited meat score	Total additives	ISAAC asthma %	ISAAC centres
UK	19.9	50	69.9	32.2	15
Australia/NZ	38.1	50	88.1	29.4	10
USA	46.2	0	46.2	21.7	3
Uruguay	9.6	50	59.6	19.0	1
Capetown (Sth Africa)	7.8	25	32.8	16.1	1
Japan	30.1	0	30.1	13.4	1
France	15.4	0	15.4	13.1	5
Spain	7.7	25	32.7	10.3	8
Hong Kong	12.4	0	12.4	9.1	1
Italy	5.6	0	5.6	8.9	13
India	0.3	0	0.3	6.0	14
Guangzhou (China)	4.9	0	4.9	3.4	1
Indonesia	0.5	0	0.5	2.1	1

Table 2 Total food additive intake score (Total additives) estimated as density of McDonald's fast food outlets per million population (McScore) added to Sulphited meat score, compared with ISAAC asthma rates in selected countries.

There were notable differences in food additive consumption between countries and regions. Scotland had the highest intake of two major sulphite vectors: daily sugared soft drink consumption by young people was the highest of 20 ISAAC countries[67] and, being the last locality in the UK to permit the use of sulphites in minced meat due to lack of refrigeration in remote regions[36], reported higher levels of sulphite overuse than England (table 1). The USA had the highest use of processed food (table 2) and a reported 'prevalence and abundance of unlabelled sulphites'[25], except for a prohibition on the use of sulphites in meat. Data was not available for present day Spanish-speaking Latin American countries. However, high sulphite use was likely, due to the rapid transition in that region from a subsistence to supermarket diet at an earlier stage of development than

in Spain[68], a strongly growing local fast food industry[53] and a traditional use of sulphite preservatives[58] combined with probable sulphite levels similar to Spain's before EU harmonization[38]. At the time of ISAAC data collection, Spain's diet was low in processed foods[63 64]and the usual drink for Spanish adolescents was water[63]. The decreasing use of sulphites in meat[35 39] was offset by an increasing intake of sulphited drinks[69]. Japanese caution regarding the use of food additives as exemplified by lower Maximum Permitted Levels (MPL) for certain sulphite use and prohibition of certain food colours[70] resulted in a lower food additive intake overall than would be expected for a wealthy country with a high density of fast food restaurants. In India, the southern state of Kerala with the best educated, most traveled and most Westernised population of the Indian states[71], had the strongest commercial beverage market of ISAAC centres[72].

There were also variations between countries in their use of other asthmagenic additives. In the USA, according to FDA data, the per capita production of artificial food colours increased fourfold[73] since the first report of colour-related asthma in children in 1958. In the UK, complaints concerning asthma related to Indian food led to the discovery that a labelling loophole permitted the excessive use of artificial colours[49] and a significant dietary intake of colours was lately been reported in India[74]. Benzoate preservatives are widely used in drinks[34], reported in seafood and medications in France[27], and permitted in sausages in South Africa[61]. Higher levels of BHT are permitted in the USA than in other countries[29]. In Australia and especially New Zealand the use of BHA is common in margarines and cooking oils except olive oil and may account at least partly for the finding that the use of margarines and cooking oils compared to butter and olive oil is a risk factor for asthma in preschoolers[75]. Annatto natural colour (E160b) which has been linked to adverse reactions in asthmatics[83] may be a particular problem in South America where it is consumed in large quantities regionally as a food seasoning[29].

Discussion:

Principal findings

Data presented relates the use of food additives, especially sulphites, with the increase in asthma associated with the Western lifestyle. Estimates show a high use in English and Spanish-speaking countries, low use in developing countries, a marked difference in NW/SE European countries; and a striking difference between Hong Kong and Guangzhou. Very young children, residents in low income areas in developed countries, the overweight, and consumers of sulphite vectors in warmer weather or without refrigeration were the groups found to be most at risk of high sulphite intake.

Recent declines in childhood asthma in the UK[4], Italy[5], Australia[6], Hong Kong[7] and Singapore[8] coincided with a reduction in consumption of sulphites and other food additives due to a variety of causes. Fluctuations in sulphite intake would not be obvious to consumers. A 30-70% increase in the amounts of several sulphiting agents used annually in the 1960s in the USA was due to the growth of the processed food industry[47] which spread to the rest of the developed world in the 1970s[76]. Following a number of asthma deaths related to sulphited salads in the USA there was a prohibition on sulphite use in fresh fruit and vegetables in 1986, which reduced the amount of sulphites consumed in a single dose[44] but was balanced overall by increasing consumption of French fries[76]. In the 1990s, food regulators in the UK, Europe and Australia worked to reduce the use of sulphites[32 34 36 40 42 62]. At the same time, the growing preference in higher income

economies, including Hong Kong and Singapore, for healthier beverages such as bottled water and pure fruit juice rather than fruit drinks and carbonated drinks[77] would contribute to reduced intake of additives. In 1993, at the peak of mad cow disease, there was a change in the nature of the British meat industry due to the decline in beef consumption[78] and a beef export ban as well as cheap imports of meat. Many small slaughterhouses were unable to cope with the EU's new hygiene regulations and supermarkets took the major share of meat sales[60] due to the decline of specialist butchers' shops, which had been nearly twenty times more likely to use sulphites illegally in mince than supermarkets[36]. In the last half of the decade, following Chinese handover, Hong Kong underwent a period of de-westernisation during which the Carrefours chain of hypermarkets closed and weekend shopping expeditions to Guangdong province's cheaper shops became popular[54].

Strengths and weaknesses of the study in relation to other studies

In the only previous evaluation of worldwide sulphite intake (WHO), information provided by 10 countries could not be compared, due to the use of different methods to estimate sulphite levels in foods, sulphite intake and consumer categories. Children were included by two countries. Estimates ranged from 5% of the ADI for Japanese adults to 11,000% of the ADI for children in the UK.

Our study is the first to attempt an international comparison of additive intake using comparable data. Our results are more reasonable than figures from the WHO survey and match more recent single country surveys[31 32 37]. McScore is more likely to be accurate in mature markets such as Europe and English speaking countries than developing markets such as South America where an extremely rapid nutrition transition led to the development of local fast food chains before the spread of McDonald's outlets. The major weakness of this study is the lack of data regarding food additive intake outside English speaking and European countries.

Future research

There is a need for more accurate figures about the actual intake of food additives by children, especially excessive consumers[32]. Ideally, each ISAAC country would assess actual sulphite contents of realistic meals, as used in recent studies of sulphite worst-case scenarios for Italian children[32] and English adults[37]. The use of other asthmagenic additives should also be considered, since the principle governing the WHO re-evaluation of the effects of sulphites on children, that children consume more relative to their weight, also applies to other food additives. If the effects of food additives are to be tested, a comprehensive food chemical elimination diet should precede challenge testing to avoid missing responders[28].

Implications for policy makers

There is no evidence for the assumption by food regulators that people prone to asthma are 'likely to avoid foods that contain sulphites'[31]. Although the increase in childhood asthma worldwide appears to have been halted in some developed countries, asthma rates remain at a higher level than in the 1970s[79]. If the food additive hypothesis is confirmed, countries may choose to reduce their use of asthmagenic food additives. According to Italian food scientists, sulphites are not always essential from a technological

point of view and MPLs could be reduced[32]. WHO guidelines state that where a suitable alternative method of preservation to sulphites exists, its use should be encouraged[29], although sulphites are not the only additives associated with childhood asthma. The cautious approach to food additives, including sulphites and artificial colours, in Japan[70] demonstrates that the use of food additives can be minimised. The appropriate public health response may be 'to remove the irritants, if possible, from the foods that children eat'[73].

What is already known on this topic

The prevalence of childhood asthma has increased over the past three decades in many countries, particularly in children under school age.

Food additives, especially sulphites, have been associated with asthma exacerbations for many years and asthmatics have been shown to improve on additive-free diets.

An upgraded World Health Organisation estimate suggests that seven times more asthmatic children are sensitive to sulphites than previously thought.

What this study adds

Consumption of food additives, especially sulphites, can explain worldwide variations in childhood asthma prevalence.

Preschoolers eating the Western diet consume more sulphites than any other age group.

The decline in childhood asthma in some countries coincides with a reduction in the consumption of sulphites.

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