volume in 1 s (FEV1) reduced to 1.7 litres (46.8% of predicted) and FEV1/forced vital capacity (FVC) ratio 55.9%. Since his RA responded favourably on adalimumab and there was not enough evidence to ascribe his respiratory complaints to this drug, it was decided to rechallenge him with adalimumab. During the third administration of adalimumab he still used prednisolone 20 mg/day and inhaled budesonide/formoterol twice daily. On the third day following adalimumab administration he developed dyspnoea, wheezing and a reduction in his PEF to 290 l/min. His PEF went back to baseline after 2 weeks.

Bennett et al reported a patient with presumed adalimumab-induced asthma. They hypothesised that once the tumour necrosis factor (TNF)α blocking adalimumab was introduced the T helper cell (Th)1 response characteristic for RA was suppressed, allowing the Th2-activated pathway to express itself as asthma. However, patients with asthma have upregulation of the existence of a class effect. Symptoms to adalimumab. This case therefore refutes etanercept, adalimumab and infliximab way to express itself as asthma.

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Figure 1 The patient was instructed to monitor his peak expiratory flow (PEF) twice a day. The first 2 days after the third adalimumab administration he had a stable PEF of approximately 450 l/min. On the third day he developed dyspnoea, wheezing and a reduction in his PEF to 290 l/min. His PEF went back to baseline after 2 weeks.

Bennett and colleagues assumed that the pathophysiological mechanism causing adalimumab was a direct effect of the TNFα blocker under strict medical observation. However, patients with asthma have upregulation of the existence of a class effect. Symptoms to adalimumab. This case therefore refutes etanercept, adalimumab and infliximab way to express itself as asthma.

Since Bennett and colleagues assumed that the pathophysiological mechanism causing adalimumab was a direct effect of the TNFα blocker, they suggested a class effect and decided not to treat their patient with other TNFα blocking agents. Our patient used etanercept, adalimumab and infliximab within a short time frame and only reacted to adalimumab. This case therefore refutes the hypothesis that the asthmatic response is caused by blockage of TNFα, as well as the existence of a class effect. Symptoms started 3 days after drug administration which is not compatible with anaphylaxis. A delayed-type T-cell mediated hypersensitivity reaction would be more likely.

At present it is unclear how often adalimumab has induced asthma-like symptoms. Because the use of adalimumab is increasing, this adverse event may become more prevalent in the future. We are the first to report adalimumab-induced bronchospasm with a positive rechallenge on the agent itself and negative challenges on etanercept and infliximab. We believe it is justified to make a switch to a different TNFα blocker under strict medical observation.

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REFERENCE


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Is bronchodilation required routinely before diagnostic sputum induction? Evidence from studies with tuberculosis

Sputum induction (SI) by inhalation of nebulised hypertonic saline is an efficient

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and non-invasive way of obtaining samples to assess airway inflammation and diagnose pulmonary infections such as tuberculosis (TB). Data published on the safety of SI are largely derived from subjects with obstructive lung disease. Yet on this basis a Working Group of the European Respiratory Society (ERS) recommended that all patients undergoing SI should receive pre-procedure bronchodilatation with monitoring throughout by either serial forced expiratory volume in 1 s or peak expiratory flow rate (PEFR) measurements. Subjects with other respiratory conditions may not be at the same risk of bronchoconstriction as the original reference group. If so, then the recommended steps could be removed from routine SI, leading to a simplified procedure with no compromise in patient safety. Here we report our findings from routine clinical practice.

We prospectively observed 100 consecutive and unselected adult subjects undergoing SI to investigate possible TB. SI was performed using 5% hypertonic saline delivered via an ultrasonic nebuliser (Sunrise Medical, Wollaston, UK). To ensure good infection control, bronchoscopy was assessed with disposable Mini-Wright peak flow meters (Clement Clarke International, Harlow, UK). PEFR was measured at baseline and then at 5, 10, 15 and 20 min. The preselected criteria for discontinuing SI were: (1) a fall in PEFR of >15% at any time point, (2) patient choice, (3) if the patient were deemed by the clinician performing the test to be unable to continue. Bronchodilators and resuscitation equipment were available if required. Equipment costs for generic salbutamol metered dose inhaler devices and the PEFR meter were covered from the British National Formulary (March 2007) and manufacturer’s data.

Most age of the 100 subjects was 43 years (range 18–68) and 60 were male. Six were ex-smokers and 26 were current smokers. Median baseline PEFR was 450 l/min (range 220–710). No subject had to stop SI. Median baseline PEFR was 450 l/min (range 220–710). No subject had to stop SI. Six were ex-smokers and 26 were current smokers. Median age of the 100 subjects was 43 years (range 18–68) and 60 were male. Six were ex-smokers and 26 were current smokers. Median baseline PEFR was 450 l/min (range 220–710). No subject had to stop SI.

Margarine: a supplement may be decisive

A recent study in Thorax described margarine intake as a risk factor for allergic diseases (Thorax 2007;62:677–83). This association has now been replicated in about 10 studies, but without any convincing explanation,1 Margarine is the only food factor to date without any convincing explanation.1 Margarine is the only food factor to date without any convincing explanation.1 Margarine is the only food factor to date without any convincing explanation. This means that farmers and margarine manufacturers need to be aware of the possible association between margarine intake and allergic disease.

Margarine was invented by the French chemist Hippolyte Mège-Mouriès at the demand of emperor Napoleon III and his army in 1869 as a cheap replacement food for his troops. The initial recipe contained water, skimmed milk and sugar. The use spread rapidly as a butter substitute, with the first factory in Oss/Netherlands exporting approximately 40 000 tons of margarine to Great Britain in 1883. As a raw material, lard was used at that time as well as copra, palm or train oil. As sales in the mid of the last century suffered from a somewhat poor quality image, modifications have been introduced, for example, to raise the content of polyunsaturated fats by using sunflower oil.

Since 1952, vitamin D3 has also been added to margarine in West Germany. According to a new monograph on the history of vitamin D supplementation in Germany,2 the company Merck delivered a highly concentrated oil vitamin solution to the Margarine Union who supplemented about the half of the 230 000 tons annually produced at that time. Since then margarine has been one of the few if not the only continuously fortified food in Germany with a major brand containing ~1 IU/g D3.

Given more recent experimental and epidemiological findings on the immunological action of vitamin D and its metabolites,3 it is possible that this vitamin D supplement may be responsible for the observed effect. Changing from butter to margarine indeed leads to ~30% higher 25-OH-calciferol serum levels4 which may be in the effective range of serum levels linked to allergic rhinitis in the NHANES study.5 Possibly a trial on the Crete island could answer the question of whether or not there is any causal relationship between a margarine ingredient and allergy. Vitamin D supplements could be banned from margarine for a limited time as on a sunny island there is no major fear of vitamin D deficiency in the population. Will the allergy risk remain?

REFERENCE


REFERENCES


Authors’ reply

We read with great interest the letter by Wjst proposing an alternative hypothesis for margarine supplementation by vitamin D as the risk factor underlying its positive associations with asthma and allergies. In our recently published study (Thorax 2007;62:677–83), we found that margarine intake was a risk factor for asthma and rhinitis symptoms among children in Crete. We hypothesised that the high concentration of n-6 PUFAs in margarine could partially explain the observed associations through modulation of the synthesis of IgE and inflammatory mediators.

The evidence regarding the effects of vitamin D on the development of asthma and allergies is controversial. Vitamin D has been shown to inhibit Th1 immune responses but its effects on Th2 responses are more complex and not fully elucidated. Moreover, genetic studies have provided early, although not clear, evidence of the
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