UNCERTAINTIES PAGE

Does avoidance of peanuts in early life reduce the risk of peanut allergy?

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Peanut allergy has increased in frequency and severity such that it is now responsible for considerable morbidity and in some cases mortality. This has led to conflicting policies aimed at reducing the risk of children developing peanut allergy. Expectant women and parents of young children, as well and their clinicians, are therefore often unclear about whether to avoid peanuts.

What is the evidence of uncertainty?

We searched the Cochrane Library and PubMed using a combination of MeSH and free text terms from the inception of these databases to November 2009 to identify relevant systematic reviews and original studies that had investigated the effect of peanut avoidance in pregnancy, in mothers who were lactating, and in the diets of infants, on the risk of subsequently developing peanut allergy. We also searched Google Scholar and online trial registries (ClinicalTrials.gov and Controlled-trials.com) to identify unpublished and ongoing randomised controlled trials.

Summary of revised advice on peanut avoidance from the Department of Health and the Food Standards Agency[10]

During pregnancy and while breast feeding

If mothers wish to eat peanuts or foods containing peanuts during pregnancy or breast feeding then they can do so as part of a healthy balanced diet, irrespective of whether their child has a family history of allergies

When introducing peanut into a child's diet

All mothers should try to exclusively breastfeed their baby for the first 6 months of life. If mothers choose to start giving their baby solid foods before age 6 months, they should not introduce peanuts or other allergenic foods (such as other nuts, seeds, milk, eggs, wheat, fish, or shellfish) before this time, and when they do, these foods should be introduced one at a time so that they can spot any allergic reaction

Additional advice

Where a child already has another kind of allergy (such as diagnosed eczema or a diagnosed allergy to foods other than peanut), or if there is a history of allergy in the child's immediate family (parents, siblings) then mothers should talk to their general practitioner, health visitor, or medical allergy specialist before giving peanut to the child for the first time because these children are at higher risk of developing peanut allergy

Changing advice on the role of peanut avoidance

In 1998 the UK government advised that those at "high risk" of developing allergy (that is, those with a family history of allergic problems) may wish to avoid eating peanuts and products that contain peanuts during pregnancy, lactation, and weaning (until infant is aged 3 years).[1] Similar advice was issued around the same time in several other countries.[2 3]

This advice on avoidance of peanuts was based on the findings of epidemiological studies, which suggested that exposure to peanuts during this "critical window" in early life may increase the risk of peanut allergy.[4 5] Supportive, potentially more compelling, evidence came from the early randomised controlled trials of avoidance of dietary allergens (including peanut) during pregnancy and/or early childhood; these trials found significant reductions in the risk of children developing allergic disease when dietary allergens had been avoided.[6 7]

This general agreement on the importance of avoiding peanuts in high risk families in early life has recently been challenged, however, by concerns that avoiding peanuts during this critical immunological window may in fact increase the risk of food allergy.[8 9] This has led to the Department of Health and the UK Food Standards Agency recently issuing revised advice (box).[10] New Zealand's Ministry of Health and the American Association of Paediatrics have also updated their advice.[3 11]

Why are there concerns about peanut avoidance?

Four key arguments have been raised. Firstly, evidence from randomised controlled trials on the effectiveness of dietary restriction during pregnancy and lactation is conflicting. A Cochrane systematic review concluded that avoidance of foods during pregnancy was unlikely to be effective and that no compelling evidence existed for mothers to avoid allergens while lactating.[12]

Secondly, an epidemiological study conducted several years after the introduction of the initial UK advice failed to show the anticipated reduction in the prevalence of peanut allergy.[13]

Thirdly, evidence exists that the original UK advice was not clearly communicated to the target population of high risk families, and this shortcoming resulted in many cases of blanket avoidance of peanuts, even in low risk families.[14]

bmj.com archive **"Not only are nuts and staples like peanut butter prohibited from campus, but so too are homemade baked goods or any foods without detailed ingredient labels. School entrances have signs admonishing visitors to wash their hands before entry to avoid contamination"** Nicholas Christakis, in "This allergies hysteria is just nuts" (2008;337:a2880)

Finally, and most fundamentally, evidence is increasing that oral exposure to allergens such as peanuts in early life may be important for inducing immunological tolerance to these foods. Particularly important in this respect has been an epidemiological study that found that the prevalence of peanut allergy was 10-fold lower in Jewish people living in Israel—where peanut butter is used in the weaning food "Bamba"—than in London based Jewish families, who had less frequent exposure to products containing peanut.[15]

Is ongoing research likely to provide relevant evidence?

Two ongoing randomised controlled trials, scheduled to report in 2013-5, should begin to provide clarity on whether or not to expose infants to peanuts in early life. The EAT trial is comparing infants introduced to allergenic foods—including peanuts—from the age of 3 months with infants in a control group who will avoid foods containing these allergens until aged 6 months.[16] The main outcome for this trial is the prevalence of IgE mediated allergy to these foods by the age of 3 years.

The related LEAP trial in high risk infants aged 4-11 months is comparing those being fed at least 6 g of peanut protein a week with those in a control group whose diet excludes peanuts. The main outcome of interest is the proportion of children with peanut allergy at age 60 months.[17]

What should we do in the light of the uncertainty?

At present, the soundest position is to advise all pregnant women who are not allergic to peanuts, irrespective of whether or not there is a family history of allergy, that there is no evidence of danger from eating peanuts. Breast feeding should be encouraged, although no clear evidence exists that avoiding peanuts during lactation will reduce the risk of peanut allergy. It is important to explain that currently we do not know the best time for children to be exposed to peanuts. In general, however, foods that are potentially allergenic are best first introduced one at a time, beginning with small quantities, when the child is otherwise well. If mothers are anxious, discussions with their general practitioner may prove useful, with testing for sensitisation to peanut if necessary.

Whole peanuts present a choking danger and should therefore, irrespective of any concerns about allergy, be avoided until children are at least 3 years old.

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LESSON OF THE WEEK

Tachycardia due to atrial flutter with rapid 1:1 conduction following treatment of atrial fibrillation with flecainide

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Flecainide can "organise" atrial fibrillation into atrial flutter with 1:1 conduction, leading to cardiovascular compromise

The treatment of atrial fibrillation in the emergency department is often complex and depends on several factors, including time of onset of atrial fibrillation and previously known cardiac disease. Current guidelines include flecainide as a possible treatment for chemical cardioversion and maintaining sinus rhythm in paroxysmal atrial fibrillation.[1 2] An important, under-recognised complication of flecainide is the transformation of rhythm from atrial fibrillation to atrial flutter. We present four such cases.

Case reports

Case 1

A 56 year old man with paroxysmal atrial fibrillation, receiving maintenance therapy of flecainide 100 mg twice daily, awoke with palpitations which felt irregular after an alcohol binge. He took an extra dose of flecainide, after which he felt his heart rate increase and become more regular (fig 1, top). At the emergency department, he was found to be in atrial flutter with 1:1 conduction at a ventricular rate of 200 beats per minute and a rate related bundle branch block. This was incorrectly interpreted as ventricular tachycardia and since he was not cardiovascularly compromised he was given intravenous sotalol. His ventricular rate slowed and revealed atrial flutter with 2:1 block (fig 1, bottom) at half the rate of the first electrocardiogram. He was subsequently electrically cardioverted into sinus rhythm with normal QRS duration.

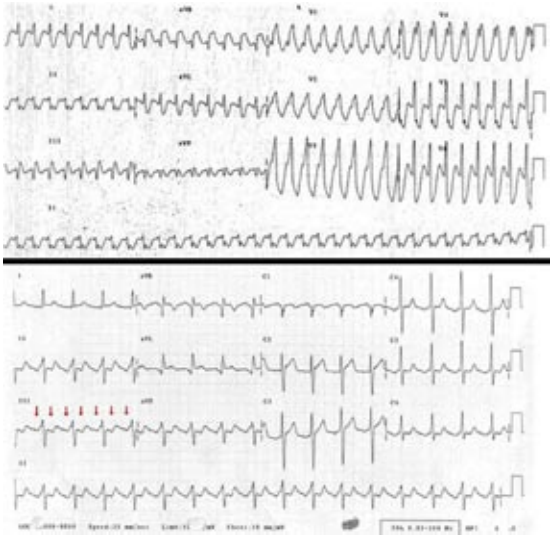

Fig 1 | Broad complex tachycardia of 200 beats per minute (top), mistaken for ventricular tachycardia. There is no evidence of independent P wave activity to suggest atrioventricular dissociation seen with ventricular tachycardia. This is atrial flutter with 1:1 atrial to ventricular conduction, and rate-related bundle branch block. After intravenous sotalol, ventricular rate slowed by half (bottom), showing the typical "sawtooth" baseline of atrial flutter waves in the inferior leads (red arrows); the electrocardiogram now shows atrial flutter with 2:1 atrioventricular block

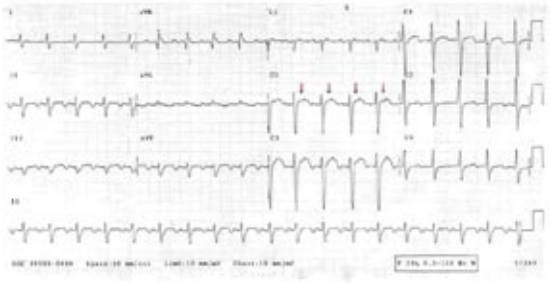

Fig 2 | In addition to an apparent P wave before each QRS complex, a flutter wave is "buried" in the T wave of the preceding complex (red arrows in V2), indicating atrial flutter with 2:1 atrioventricular block

Case 2

A 60 year old man receiving flecainide for paroxysmal atrial fibrillation presented to the emergency department with an episode of collapse with loss of consciousness. He had had a similar episode four weeks previously, after which his daily dose of flecainide was increased by his general practitioner. On arrival at the emergency department, he was fully conscious, with a Glasgow coma score of 15. His electrocardiogram (fig 2) indicated that he was in atrial flutter, with 2:1 block and a ventricular rate of 100 beats per minute.

Case 3

A 56 year old woman had a presyncopal episode associated with shortness of breath. On arrival at the emergency department she was found to be in atrial flutter with variable block and a ventricular rate of 96 beats per minute (fig 3, top). She had had a similar clinical episode two weeks before, after which she had been given regular flecainide in primary care at a dose of 50 mg twice daily. One hour after a further oral dose of flecainide, she developed rapid 1:1 conduction associated with atrial flutter (fig 3, bottom) and worsening symptoms. Direct current cardioversion successfully reinstated sinus rhythm.

Case 4

A 57 year old woman with a history of paroxysmal atrial fibrillation treated with flecainide and metoprolol attended the emergency department. Her initial electrocardiogram

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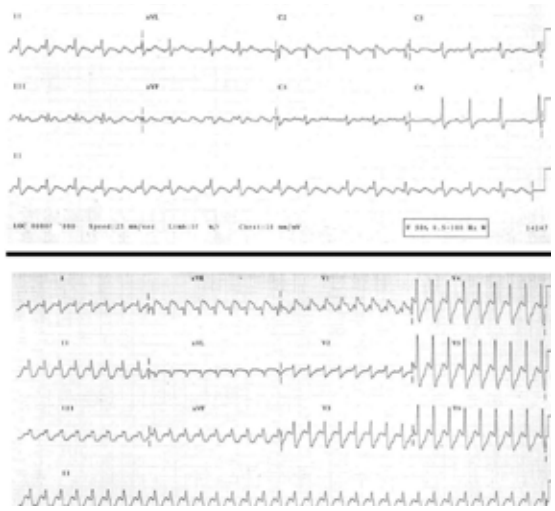

Fig 3 | Atrial flutter with variable block in a patient given flecainide in primary care: (top) the sawtooth baseline is evident in the inferior leads (II, III, and aVF). After a dose of oral flecainide in the emergency department the patient developed a tachycardia at 201 beats per minute consistent with atrial flutter with 1:1 conduction, and underwent direct current cardioversion. An electrocardiogram in sinus rhythm (bottom) showed incomplete right bundle branch morphology associated with a known atrial septal defect (sodium channelopathy was considered unlikely)

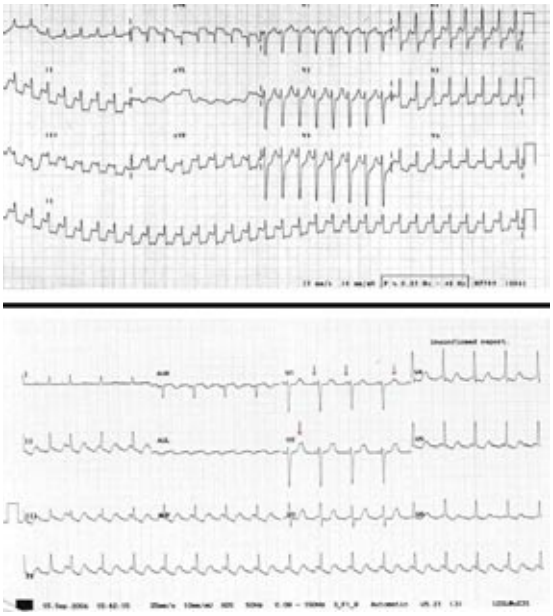

Fig 4 | The differential diagnosis of regular narrow complex tachycardia includes supraventricular tachycardia (atrioventricular re-entry tachycardia) due to an accessory pathway. Atrial conduction velocity is slowed by class 1c agents such as flecainide, producing pro-arrhythmias with 1:1 conduction (top) at a slower rate of about 200 beats per minute, in contrast to typical atrial flutter, which usually occurs at 300 beats per minute. After sedation, the patient's ventricular rate slowed to 100 beats per minute, showing the typical sawtooth baseline of atrial flutter, with 2:1 block, in the inferior leads (bottom); this was initially misinterpreted as sinus rhythm on limited examination of monitored leads V1 and V2, where atrial depolarisation before each QRS complex seems to be a P wave (blue arrows); closer inspection shows flutter waves producing notched T waves (red arrows), in addition to the sawtooth baseline in the inferior leads

showed atrial flutter with 1:1 conduction (fig 4, top). Sedation with propofol for direct current cardioversion resulted in 2:1 block (fig 4, bottom). This was misinterpreted as sinus rhythm. She subsequently reverted to atrial fibrillation.

Discussion

Flecainide is a class 1c antiarrhythmic agent which acts by inhibiting sodium channels and slowing conduction velocity. It is used for maintaining sinus rhythm in paroxysmal atrial fibrillation and for chemical cardioversion in patients presenting with new onset atrial fibrillation. In the acute setting, it can be given as an intravenous infusion, but it is increasingly given orally when there are no signs of cardiovascular compromise. A single dose "pill in the pocket" approach has been recommended for selected patients.[1]

These cases underline an infrequent but clinically important consequence of using flecainide, namely the "organisation" of atrial fibrillation into atrial flutter.[3] Slowing of conduction results in a slower atrial flutter rate with the proarrhythmia, at about 200 rather than 300 beats per minute; this facilitates 1:1 conduction through the atrioventricular node, resulting in a rapid ventricular response and potential cardiovascular compromise.[4 5] Thus when 2:1 conduction occurs, the electrocardiogram may show a regular ventricular rate of 100 beats per minute, rather than the typical 150 beats per minute seen when the atrial rate is 300 beats per minute; this recognition can be a useful clue in interpreting tachycardia on electrocardiograms in primary care and emergency departments. Other rhythm disturbances that can occur with flecainide include atrioventricular block, sinus pauses (particularly on termination of atrial fibrillation), and ventricular tachycardia.

The occurrence of proarrhythmia with flecainide is reduced by avoiding using the drug in patients with bundle branch block and structural heart disease, including important valvular or ischaemic heart disease, left ventricular hypertrophy and dysfunction. The use of an atrioventricular nodal blocking agent in conjunction with flecainide also reduces occurrence of the proarrhythmia.

This case series highlights the need to be vigilant of the clinically important proarrhythmic effects associated with flecainide, a drug increasingly used in primary care and emergency departments. Flecainide can "organise" atrial fibrillation into atrial flutter with tachycardia due to rapid 1:1 atrioventricular conduction; the ventricular rate may be slower than that normally expected. Concomitant use of a β blocker (bisoprolol, for example[2]) is recommended to prevent this complication.

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