Where now with cramp?

Dear bpac

We are having prescribers declining to continue quinine prescriptions for cramp, yet unable to offer any alternative beyond referral to us for OTC products. What is the current "Best Practice" for treatment of night cramp in the elderly?

Bruce Stimpson, MPS

The short answer is that unfortunately there is no real alternative to quinine for treating cramp.

There have been both local and international reports of thrombocytopenia associated with quinine use. This is thought to be an idiosyncratic hypersensitivity reaction which has a short time to onset and can be severe. Discontinuing quinine, should symptoms of thrombocytopenia occur, may not necessarily prevent serious consequences. For these reasons quinine is no longer indicated for the treatment of leg cramps.[1]

The first step for treating cramp is to exclude other possible causes. Some medicines that have been reported to cause leg cramp include diuretics, calcium channel blockers (especially nifedipine), beta-agonists, steroids, and fibrates.[2, 3, 4] Medical conditions associated with leg cramps include fluid and electrolyte disturbances, uraemia, diabetes, and thyroid disease.[2 ,3 ,4]

There are limited options to prevent leg cramps however some suggestions include:[2, 3, 4, 5]

- General measures to improve sleep such as avoiding alcohol and caffeine-containing drinks before bed, and not going to bed until tired.
- Stretching calf and foot muscles before going to bed and intermittently during the day.
- Drinking plenty of fluid during the day to avoid dehydration. But avoid drinking too much as this can dilute the concentration of sodium in the blood which can also cause leg cramps. About six to eight glasses may be appropriate.
- Wearing good shoes may help as flat feet and other structural problems may make some people more susceptible to leg cramps.
- Avoiding tight or heavy bed covers may help as this can tighten calf and foot muscles. Loosening the covers or sleeping on the stomach with feet hanging over the bed can keep muscles relaxed.

While there is limited evidence of the effectiveness of these measures they are generally safe and worth suggesting to patients suffering from leg cramps.

Dietary supplements such as magnesium and vitamin E have been suggested as possible remedies for leg cramps however the evidence of their effectiveness is lacking.[6]

Note: tonic water contains a very small amount of quinine. There have been isolated reports of adverse effects such as thrombocytopenia and skin reactions in people drinking large quantities, however, this is rare. Consuming normal quantities is unlikely to offer any benefit for treating leg cramps.

References:

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6. Clinical Evidence. BMJ Publishing Group Limited 2008. Available from http://clinicalevidence.bmj.com/ceweb/conditions/msd/1113/1113.jsp (Accessed January 2008)

Should we prescribe fibrates?

Can't quite get my head around whether consensus is that fibrates are a waste of time and money in everyone nowadays or if there may still be subgroups of hyperlipidaemics who might derive benefit. Have you come across any reviews that may help?

Patch Graham.
GP, Nelson

Large trials of fibrates in recent years have generally shown significant positive changes in lipid levels however this has not consistently resulted in a reduction in cardiovascular events or all-cause mortality. Overall most trials have shown a trend towards a reduction in non-fatal cardiovascular events but most have not shown a significant reduction in mortality. This coupled with increasing evidence for statins to prevent cardiovascular events has resulted in a limited role for fibrates.[1,2,3]

Some guidelines suggest that fibrates may be used:

- As first-line therapy for severe hypertriglyceridemia (10 mmol/L or more), as these individuals are at high risk of pancreatitis.[2]
- For patients with high cholesterol only if other effective agents, such as statins, are contraindicated or not tolerated.[2]
- In combination with a statin for mixed dyslipidaemia that has not responded to initial statin therapy. However this combination must be monitored and is best initiated by a specialist as it carries an increased risk of muscle-related adverse effects such as rhabdomyolytis.[3]
- For some subgroups of patients such as those with type III genetic dyslipidaemia which is rare.[4]

References:

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Safety of LABAs

I was surprised to find no mention of the increased risk of asthma exacerbations and asthma-related deaths with the use of LABAs in your article on Symbicort Maintenance and Reliever Therapy.

The Salmeterol Multicenter Asthma Research Trial (Chest 2006;129;15-26), which compared the safety of salmeterol or placebo added to usual asthma care, showed a two-fold increase in life threatening asthma exacerbations and a four-fold increase in asthma-related deaths in the salmeterol group.

A meta-analysis of the effect of LABAs on severe asthma exacerbations and asthma related deaths (Ann Intern Med. 2006;144:904-912) also found a 3.5-fold increase in asthma related deaths, a 2.6-fold increase in exacerbations requiring admission and a 1.8-fold increase in life-threatening exacerbation with the use of LABAs.

It is suggested that this increased risk is not seen with concomitant use of inhaled corticosteroids. However, in the above meta-analysis, when the evaluation was restricted to studies in which >75% of participants used inhaled

corticosteroids, a four-fold increased risk of hospitalisation was still demonstrated in the LABA treated group.

It seems that there is still sufficient concern about the safety of these agents to advise caution in their use even when combined with an inhaled steroid. The increase in their administration which is likely when used as part of the SMART regimen is therefore worrying and, I believe, warranted a mention in your article.

GP, Christchurch

Yes we agree, and it is possible that the effectiveness of the SMART regimen may be partly due to the change in use of corticosteroids. People may receive corticosteroids earlier in an exacerbation with the new single inhaler technique.

As you state, it appears from the recently published SMART trial, that LABAs may increase the risk of severe asthma exacerbations or death, particularly in those people on LABA monotherapy or of African American descent.[1]

Your letter has given us the perfect opportunity to reiterate the advice we gave in BPJ 2 (December 2006), where we included an update on the use of LABAs for the treatment of asthma. Our key points in that article were:

- Long acting beta agonists (LABAs) are not indicated as first-line therapy for any asthmatic patient.
- Adverse reactions to LABAs such as hyper-responsiveness, bronchospasm and respiratory arrest are rare but patients should be closely monitored for the first 6 - 12 weeks after the initiation of treatment.
- LABAs should only be prescribed for people who are already on inhaled corticosteroids (ICS).
- LABAs may be indicated as add-on therapy if symptoms do not respond to low to moderate doses of ICS (e.g. in adults 400 - 800 micrograms beclomethasone or equivalent).
- Patients on LABAs should be counselled and reminded of the importance of continuing their ICS.
- LABAs should be discontinued after a trial period if no benefit is seen.
- Patients with acutely deteriorating asthma should not be started on a LABA.
- Review the asthma management plans of people on combination LABA/ICS inhalers.

The November 2007 Prescriber Update contained a similar reminder about safe prescribing of LABAs and gave the following advice: [2]

- LABAs should not be used as monotherapy or first-line treatment for asthma; a LABA should be added to asthma treatment only if an appropriate dose of an inhaled corticosteroid does not provide adequate control.
- Patients should be warned not to stop or reduce corticosteroid therapy without medical advice, even when symptoms improve.
- LABA therapy should not be initiated, or the dose increased, in patients with significantly worsening or acutely deteriorating asthma.
- Patients should be advised to seek medical attention immediately if their asthma deteriorates suddenly.
- A reassessment of therapy should be undertaken if asthma worsens despite regular use of a LABA and an inhaled corticosteroid.

References:

1. Nelson H, Weiss S, Bleecker E, et al. The salmeterol multicenter asthma research trial: A comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest 2006; 129: 15-26.

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