

# Prescribing...

## Hot Therapeutic Topics II

- April's bulletin looks at three more topical pieces of research.
- The use of Diclofenac, but not other NSAIDs, may be linked to a modest but significant increased risk of *C. Difficile* infection.
- "Mental exercise" may boost cognitive function in people with dementia.
- According to a large cohort study from Denmark, the absolute risk of children developing febrile convulsions after pertussis vaccination is 4 seizures per 100,000 vaccinations.

### 1. Diclofenac and *Clostridium difficile* infection

Several case reports over the past 30 years have suggested that there may be a link between the use of Diclofenac and risk of *C. Difficile* infection. To investigate this, researchers analysed data from the UK's General Practice Research Database on all reported infections occurring between 1994 and 2005.

In total 1,306 cases were identified and matched with 13,072 controls. For each case, up to ten control patients were selected from the same GP practice. Amongst cases 7.1% had used Diclofenac within 90 days of their diagnosis, compared with 4.2% of controls during the same period. This translated into a 35% relative increased risk, after adjusting for factors such as age, associated GI diseases, co-morbid conditions and use of medicines associated with possible increased risk of *C. Difficile*. The association persisted when non-hospitalised patients were looked at separately.

There was no association between the use of other prescribed NSAIDs and increased infection risk, and there did not appear to be any link with the dose used.

#### Comment

*Of all of the NSAIDs Diclofenac is considered to have the highest risk of causing extra cardiovascular events. This new evidence suggests a link between Diclofenac use and C. Difficile infection, but it does not prove causality. However it does add weight to the recommendation that doctors should critically review the place of Diclofenac, and suggests that other NSAIDs (e.g. naproxen or ibuprofen) should be considered first-line.*

### 2. "Mental exercise" and dementia

Increasing physical and mental activity is highly beneficial in terms of maintaining physical and emotional health. Performing structured "mental exercise" through a cognitive stimulation programme improves cognitive function for people with mild-to-moderate dementia, according to a Cochrane review.

A lack of cognitive stimulation is widely accepted to hasten mental decline in older people in general and is particularly significant in people with dementia. Cognitive stimulation therapies are designed to provide general stimulation for thinking, concentration and memory through pleasurable activities such as discussion of past and current events, word games and mentally engaging tasks such as baking.

In the latest review, researchers performed a meta-analysis of fifteen RCTs involving 718 patients with mild-to-moderate dementia. On tests of cognitive function, a clear benefit was found for cognitive stimulation compared with control. The standardised mean difference (SMD) was 0.41 and this persisted after 1 to 3 months of follow-up.

Secondary analyses based on smaller samples found that cognitive stimulation was associated with gains in quality of life and well being (SMD of 0.38) and improvements in staff ratings of communication and social interaction ( SMD of 0.44). These findings suggest that the improvements in cognition as a result of "mental exercise" may have clinical significance for patients.

Researchers also found that the finding of benefit was consistent across all care settings i.e. hospital, care home, nursing home, day centre, outpatient settings and that the interventions could be offered by staff, volunteers or family caregivers to either groups of patients or to individuals.

#### **Comment**

*NICE states that all patients with mild-to-moderate dementia of all types should be offered the opportunity to participate in a structured group cognitive stimulation programme. These findings confirm the value of such programmes and show that they can improve cognition and may enhance quality of life.*

### **3. Febrile seizure rate with pertussis vaccine quantified**

Whole-cell pertussis vaccine was known for increasing the risk of febrile seizures amongst children, at a rate of about 1 in 900 vaccinations. Since the introduction of the acellular pertussis vaccine, the risk is likely to have decreased, but there has been few studies estimating the numbers for the current combined vaccination of DTaPIPv-Hib.

In a population-based cohort study, researchers looked at 6 years' data from Denmark, calculating the risk of febrile seizure within a 1-week exposure period, starting from the day of vaccination, compared with non-exposed periods. Researchers also did a self-controlled case series, based on children from the cohort who had febrile seizures.

Children did not have an increased risk of febrile seizure during the 7-day period following vaccination but there was an increased risk of febrile seizure for the day of vaccination, for the first and second scheduled dose.

This equated to an absolute risk of less than four febrile seizures for every 100,000 vaccinations. The study included 378,834 children and was based on data from the Danish Health Insurance Registry. The data from the self-controlled case series produced results similar to that of the cohort study.

#### **Comment**

*This large population-based study found a relatively low level of febrile seizures linked to vaccination. However it did find a spike in seizures in the day of vaccination, especially for the first dose of the vaccine. Clinicians may wish to remind parents of the possibility of this alarming but usually harmless reaction.*

**Written by: Geraldine O'Riordan, Prescribing Advisor Tel: 01481-732460**

**Reference: Drugs and Therapeutics Bulletin April 2012.**