Therapeutics Today

May 2020
Number 5

COVID-19 and medicines. As noted in the 2 previous editions of the Therapeutics Today newsletter, there are many useful resources available on COVID-19 and medicines. Readers are reminded of the HSE library (www.hselibrary.ie) which contains a repository of COVID-19 clinical guidance and latest research evidence. Recently updated research evidence summaries include:

- Clinical evidence for the use of antivirals in the treatment of COVID-19 (version 6, 8th May 2020)
- Clinical evidence on the use of pharmacological prophylactic therapy in healthcare workers or contacts of cases of COVID-19 (version 3, 1st May 2020)

Use of injectable steroids for hay fever? It is estimated that up to 25% of people in the UK suffer from hay fever, of which 10% remain symptomatic after using over-the-counter medicines. Intramuscular (IM) triamcinolone acetonide (not authorised in Ireland for this indication) was commonly prescribed for hay fever in the UK, however a review of the evidence in 1999 concluded that the risks outweighed the benefits ***(Drug Ther Bull 1999;37:17-18)***. A further review of the evidence for use of triamcinolone injections in hay fever was recently published ***(Drug Ther Bull April 2020;58(4):57-59)***. The DTB review includes a systematic review from 2005 (n=18 studies) which assessed the efficacy and safety of a single dose of an IM injection of corticosteroid (dexamethasone, betamethasone, methylprednisolone or triamcinolone) for hay fever. This 2005 systematic review found that there was a statistically significant effect on symptom relief which lasted from 3 to 5 weeks. Adverse events included injection site reactions, menstrual irregularities, flushing, tiredness, nervousness and minor short lasting reduction in serum cortisol. Limitations of the studies included in the systematic review were that only a minority of patients had severe disease and the majority of studies had outcomes that were based on patients' subjective assessment of relief of their symptoms, rather than well-validated scores. The authors acknowledged that there was a lack of evidence for the intervention and a need for a comparison with first line therapies. In addition, it is worth noting that patients with severe disease may require several injections which increases the risks of adverse events. An observational retrospective Danish study (published in 2013) which compared depot corticosteroids with immunotherapy for allergic rhinitis, found that regular use of depot corticosteroid injections is associated with an increased risk of diabetes and osteoporosis compared with immunotherapy. The British Society for Allergy and Clinical Immunology guideline (2017) recommends intranasal corticosteroids as first line therapy for moderate to severe persistent symptoms of allergic rhinitis. Systemic corticosteroids are rarely indicated, however if required (e.g. severe nasal obstruction), the guideline recommends a short course of oral corticosteroids over depot injectable preparations (which cannot be removed if adverse effects occur). Allergen immunotherapy is recommended as an option for patients requiring frequent oral corticosteroids. An International Consensus Statement on Allergy and Rhinology was published in 2018 which assessed the evidence for use of injectable corticosteroids for allergic rhinitis. It concluded that the adverse events (e.g. adrenal suppression, growth suppression, osteoporosis, hyperglycaemia) of injectable corticosteroids outweigh the clinical benefits, and they are not recommended for routine treatment of allergic rhinitis.
The authors of the DTB recent review concluded that **topical corticosteroids are the mainstay of anti-inflammatory treatment of allergic rhinitis** and that for people with severe nasal obstruction, a short course of oral corticosteroids is recommended over a depot injectable.

Pregabalin and gabapentin are primarily anticonvulsant drugs, which are increasingly prescribed for pain. Pregabalin and gabapentin are gabapentinoids which bind to the α 2-delta subunit of voltage gated calcium channels; this results in a decreased release of glutamate, noradrenaline and substance P, which is believed to contribute to their anticonvulsant, analgesic and anxiolytic actions. The use of gabapentinoids in pain was recently reviewed ***(BMJ 2020;369:m1315)***. Evidence supports the use of gabapentinoids to improve pain in patients with post-herpetic neuralgia or diabetic peripheral neuropathy, however **they are not effective for low back pain, sciatica, spinal stenosis or episodic migraine**. International guidelines recommend gabapentinoids as a first line treatment for neuropathic pain however there is concern regarding their increasing use, especially when used concurrently with opioid analgesics or benzodiazepines. Other first line drugs used to treat neuropathic pain such as tricyclic antidepressants and serotonin-noradrenaline reuptake inhibitors have smaller numbers needed to treat than gabapentinoids. Adverse events (AE) with gabapentinoids are common, with approximately **two in three patients (who use the drugs for neuropathic pain) experiencing an AE**; the most common AEs include dizziness, somnolence and gait disturbance. Population studies have also reported a potential for serious harms; an increase in intentional poisoning and pregabalin related deaths is associated with increased use of pregabalin, especially when co-prescribed with opioids, benzodiazepines and illicit drugs. **There are also risks of gabapentinoid misuse and dependency, which is higher in people with opioid use disorders.** Caution is advised when prescribing gapabentinoids; patients should be informed of the risks associated with their use. The use of gabapentinoids for non-neuropathic pain is not advised and there is no evidence to support combination pharmacotherapy. Patients may require a trial of six to eight weeks to determine if the benefits of the drugs justify the potential harms (e.g. suicidal behaviour, misuse or dependence). The Summary of Product Characteristics which has full prescribing information should be consulted prior to commencing treatment. Patients should be followed up to assess the response to treatment and any emerging AEs. Stopping the drug (by gradually tapering) should be considered if there is no response to treatment and/or the patient experiences AEs that interfere with quality of life.

[**Editor's note**: The HSE's Medicines Management Programme published a Prescribing Tips and Tools on the appropriate prescribing of pregabalin. It is available on ***https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/prescribing-tips-and-tools/appropriate-prescribing-of-pregabalin-.pdf]***

Teratogenicity of valproate-containing medicines (Epilim▼). The Health Products Regulatory Authority (HPRA) reminded healthcare professionals (HCPs) of important restrictions for use of valproate-containing medicines in women and girls ***(HPRA May 2020 Drug Safety Newsletter 97th Edition)***. **Studies have reported that children exposed in-utero to valproate-containing medicines have up to a 30 to 40% risk of a developmental disorder** (including delays in early development, lower intellectual abilities, poor language skills and memory problems) **and an approximate 10% risk of congenital malformations** (including neural tube defects, facial dysmorphism, cleft lip and palate, craniostenosis, cardiac, renal and urogenital defects). Population based studies show that exposed children are at an increased risk of autistic spectrum disorder and of developing symptoms of attention deficit/hyperactivity disorder compared to the unexposed population. The risks of adverse effects on exposed children seem to be dose-dependent however a threshold dose cannot be established below which no risk exists. The product information for Epilim▼ was recently updated to reflect emerging scientific evidence that in utero exposure may result in hearing impairment or deafness. In view of the known teratogenic effects, **Epilim▼ should not be used in female children and women of childbearing potential (WCBP) unless other treatments are ineffective or not tolerated**. Use of Epilim▼ in WCBP in any indication (epilepsy, bipolar) is contraindicated unless the conditions of a pregnancy prevention programme (called **prevent**) are fulfilled; treatment must be initiated and supervised by a specialist.

[**Editor's note**: Further information on the restrictions for use of valproate-containing medicines and the valproate pregnancy prevention programme (**prevent)** is available on the HPRA website (www.hpra.ie), in the Summary of Product Characteristics of Epilim▼ and in educational guides for HCPs]

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. **This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept. of Therapeutics Trinity College, Trinity Centre, SJH.** Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie @NationalNmic