Q1 Are the EPS side effects of metoclopramide more common at certain dosages?

Various sources report that dystonic side effects occur in ~25% of children and young adults (i.e. <30 years old) when high dose (2mg/kg/dose) intravenous (I.V.) metoclopramide is given as prophylaxis for chemotherapy induced nausea and vomiting as compared to adults ≥ 30-35 years old, where the incidence is reported to be ~1-2%.1,2 There are cases reported in the literature of side effects, including dystonic reactions, Parkinson-like reactions, and tardive dyskinesia, occurring with oral doses from 15 mg/day and up.3,4,5,6 A retrospective case-controlled study published in JAMA in 1995 compared New Jersey Medicaid and Medicare patients on metoclopramide with those not on metoclopramide with respect to new prescriptions for medications containing levodopa. The odds ratio for patients on 10-20 mg of oral metoclopramide to be prescribed a levodopa containing medication was 3.33 (95% CI 1.98-5.58) and 5.25 (95% CI 1.16-8.50) for patients taking >20 mg per day.7

Q2 Are there specific risk factors for metoclopramide-induced EPS?

As stated above, children and young adults experience higher rates of dystonic reactions following high dose (2mg/kg/dose) I.V. metoclopramide. When considering oral regimens of metoclopramide, increasing age, female gender, affective disorder, and the dose and duration of treatment have been reported to be risk factors for the development of EPS.8 Increasing age, female gender, length of therapy, and total cumulative dose have been reported as risk factors for the development of tardive dyskinesia. Duration of treatment prior to the onset of tardive dyskinesia has been reported to range between 4 weeks to 37 months with the average onset with in 13 to 16 months.8

Q3 Are EPS associated with metoclopramide permanent in some patients?

Dystonic reactions seen in children and young adults following high dose I.V. metoclopramide are reported to subside after the use of anticholinergic agents, such as diphenhydramine or benztropine.1,2 Parkinson-like reactions have been reported in tertiary references to resolve within 2 to 3 months following discontinuation of the drug. Cases reported in the literature have documented such symptoms lasting for 10 days after discontinuation to up to 36 months.3,4,5,6,9 Tardive dyskinesia from the use of metoclopramide has the potential to be irreversible. The risk of developing and the likelihood of tardive dyskinesia being irreversible is believed to increase with increasing duration and total cumulative dose.1,2 Tardive dyskinesia has been reported to occur after relatively short periods with low doses, however these cases appear to be more readily reversible.1

References: