A decade of Australian methotrexate dosing errors

In reply: We thank Gupta and colleagues for their comments on our article[1]. We read with interest the recommendations by the Australasian Psoriasis Collaboration of specified dosing with methotrexate Mondays and folate Fridays. This is an extension to the "name the day" recommendation set out by the Therapeutic Goods Administration in 1998.[2] However, there are concerns with naming Mondays, as this has been mistaken for "mornings" and has been the cause of previous daily dosing errors.[3] We welcome any efforts aimed at reducing inadvertent daily dosing; however, as outlined in our article, we believe that more needs to be done. Despite the fact that the recommendations of the Australasian Psoriasis Collaboration were released in 2014, we have seen an increase in dosing errors reported to the Australian Poisons Centres in 2014–2015.

Once weekly intramuscular and subcutaneous injection of methotrexate would indeed be unlikely to result in daily dosing errors; however, the poisons centres have received calls about 2- to 10-fold for intramuscular and subcutaneous dosing errors. While acute double doses of oral methotrexate are unlikely to be a problem, due to low bioavailability of doses above 25 mg, parenteral administration of a higher dose bypasses this and may be more problematic. In addition, this may be a more costly option, and injections are less acceptable to some patients. While parenteral methotrexate is useful to reduce gastrointestinal symptoms, studies have shown that folate co-prescription can reduce gastrointestinal adverse events by 80%.[4]

We believe that intentionally spreading the weekly dose out over several days should be approached with extreme caution. We acknowledge that dividing larger doses over a period of 24 hours is within current guidelines. Split doses can overcome problems with low bioavailability and may improve tolerability. Spacing by 8 hours appears to be enough to improve bioavailability.[5] We are not aware of any evidence to suggest a benefit of spreading this out over longer periods, such as several days, and our study shows clear potential for harm, with deaths occurring from low cumulative doses (eg, 5 mg daily for 5 days). In addition, splitting the dose increases the complexity of the regimen and may increase chances for error. Indeed, there has been a report of confusion regarding the split dosing schedule resulting in death.[3] ■

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