22

Modifiable predictors of hepato-toxicity in a new 'complex' drug

G. RAMNATH, S. SHAKIB, N. GRGURINOVICH, P. BAMPTON

Departments of Clinical Pharmacology and Gastroenterology, Flinders Medical Centre, Adelaide, Australia

Hepato-toxic reactions to therapeutic drugs, especially those with complex pharmacokinetics, are widely recognised and are a significant cause of morbidity worldwide. We have seen a significant number of predictable toxic reactions in spite of open access monitoring and review services. We hypothesized that many toxic reactions rise from a *few* key deficits in information.

Aim To identify key factors in drug use leading to toxicity.

Method We used Perhexiline, a drug with hepatotoxic properties, as a model. Dose modification and follow up of Perhexiline is complicated by nonlinear kinetics, a long and variable half life, genetic polymorphism in clearance, and the potential for drug interactions. We randomly interviewed doctors who requested Perhexiline levels from our lab. Using the scenario of a patient with a subtherapeutic Perhexiline level, we analyzed their knowledge of its pharmacokinetics.

Results 64 prescribers were interviewed. Based on the recommended dose adjustment, 60% (39/64) of those surveyed used potentially toxic dose modifications. Allowing for 4–6 weeks as an adequate time to approach steady state in the majority of patients, more than 50% of responders would have checked and altered dose in a potentially harmful time frame. Only 15.6% (10/64) were able to name a drug with potential interaction with Perhexiline. Of the 54 who were not aware of drug interactions, 4 drug interactions were identified on review of their patient's medication list.

Conclusion:Toxicity was predicted by a *few key deficits* in spite of the complex nature of the drug. These are: 1. when to change the dose, 2. Magnitude of dose adjustment, and 3. the most common drug interactions.

23

Eradication of *Dientamoeba fragilis* can resolve IBS-like symptoms

TJ BORODY, EF WARREN, A WETTSTEIN, G ROBERTSON, P RECABARREN, A FONTELA, K HERDMAN, R SURACE

Centre for Digestive Diseases and Concord Repatriation Hospital, Sydney

Background The role of *Dientamoeba fragilis (Df)* in gastrointestinal (GI) pathology remains controversial. It is never detected in fresh, unfixed stool specimens. Although often dismissed as nonpathogenic, this parasite can cause infectious colitis. Thus *Df* is may also be responsible for other nonspecific GI conditions.

Aims To compare *Df* detection using fresh, unfixed stools vs. fixed specimens. To determine the effect of eradicating *Df* in patients with chronic IBS-like symptoms.

Methods Twenty-one patients (6 m, 15 F; 7–78 y) presented with a 2 mth to life-long history of IBS-like symptoms including diarrhoea (2–15 motions/day), constipation, abdominal cramping, bloating, flatulence, nausea, fatigue, anorexia. All were positive for *Df*. Three stool samples from each patient collected in sodium acetate/acetic acid/formalin (SAF) fixative were examined for ova, cysts and parasites. Unfixed stools from the same samples were also examined.

Patients were treated with iodoquinol (630 mg tds) and doxycycline (50 mg bd) for 20 days. Stools were re-tested for *Df* at 4 week post-treatment and symptoms reassessed.

Results All SAF-fixed stools were positive for *Df*, while no *Df* diagnoses were made using fresh stool specimens. Eradication of *Df* was confirmed in all patients after treatment. Side-effects included dizziness, headache, nausea, lethargy and pruritus. All completed therapy. In 14/21 (67%), irregular bowel habit immediately resolved to 1–2 motions/day and improvements in other symptoms were maintained at 4 weeks posteradication. Five patients failed to report a significant change suggesting another cause for their symptoms.

Conclusions (a) The use of SAF fixative is crucial in the detection of *Df.* (b) There is a pathogenic role for *Df* in the initiation and persistence of GI symptoms. (c) Combination of iodoquinol and doxycycline gives high *Df* eradication efficacy with an acceptable side-effect profile. (d) IBS should not be diagnosed until SAF-fixed stool examination has excluded the presence of *Df.*