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Editorial

COMPOUNDING OF ORAL LIQUIDS FOR CHILDREN – RECOGNISE AND MINIMISE THE RISKS

David J Woods

Compounding (alternatively known as manipulation or extemporaneous dispensing) of medicines commonly occurs in hospital and community pharmacy. Practices include dilution and mixing of injections, mixing of topical preparations, compounding of multi-ingredient solid dose forms and the preparation of oral liquid doses forms for children.

Compounding is associated with risks to the patient and there are concerns about the quality, stability, safety and effectiveness of the final product[1]. The practice involves preparation of an unlicensed medicine with often limited information on chemical or physical stability or the potential for microbial contamination. Compounding is also inherently prone to medication errors as it involves calculations of dose per unit volume and may require special measurement techniques during administration. Most of the attention has focused on the risks associated with compounding parenteral products as adverse events tend to be more obvious and immediate. Adverse events associated with compounding of injectable products have involved calculation errors and contamination with pathogenic micro-organisms[2].

Recent reports of adverse events and medication errors involving compounded oral liquids for children have also raised awareness of the potential problems associated with this common practice. Serious toxicity in children has occurred with compounded flecainide oral liquid due to calculation errors or precipitation and erratic dosing due to fluctuating storage temperature[3, 4]. A child suffered serious baclofen toxicity due to a dispensing mix up when baclofen was used instead of sodium bicarbonate in an omeprazole mixture – baclofen was confused with bicarbonate[5]. In Canada a child died when baclofen was used instead of tryptophan powder in compounding a regular sleep medication[6].

In New Zealand the Pharmacovigilance Centre has received a number of reports of adverse events associated with compounded products. Interestingly, several of our reports have involved compounding errors with baclofen and flecainide. These drugs pose a particularly high risk when compounded as they have a narrow therapeutic index and the consequences of overdose are serious and potentially fatal.

Variability in compounding practice is also a potential source of errors as patients may receive a different concentration as they move between health facilities[7]. In some markets both a commercial product and compounded preparations are available in different strengths which is another source of confusion.

Risks of compounding can be categorised as clinical and technical[8]. Clinical risk is the consequence of receiving a sub-therapeutic or toxic dose thus the clinical risk is high with drugs such as phenobarbital, baclofen, flecainide, warfarin and beta-blockers. Technical risk is the chance of sub-therapeutic or toxic dose occurring, thus chemical or physical instability, potential for medication error, incorrect storage or administration errors may all contribute to this risk. The overall risk of the formulation is the combination of clinical and technical factors and pharmacists are in a good position to manage this risk and prevent harmful events.

Recommendations to minimise risk associated with compounded oral liquids

1. Before compounding an oral liquid carry out a risk assessment and consider strategies to manage these risks. Be especially vigilant of the potential for adverse events with high risk medicines and use commercial preparations or therapeutic alternatives if possible to reduce compounding-related risks.

2. Use standardised and validated formulas where these are available. A number of countries have standard batch sheets available and most refer to published studies carried out using commercially available suspending bases[9,10,11]. Use formulas as stated with no substitutions or changes to strength or to storage conditions as any changes can affect stability.

3. Check calculations carefully and always double check doses with a reputable resource.

4. Do not modify the strength that the patient/caregiver has been used to unless there is a clear reason to do so. The patient should always take the same strength (the standardised strength) if possible. If changes have to be made counsel carefully to ensure all changes are understood.

5. Inform patients/caregivers to report immediately any changes they observe in the oral liquid. These include appearance of cloudiness, particles, precipitation, changes in colour, smell or taste. If suspensions become difficult to suspend, e.g. with excessive caking, they should not be used and reported to the pharmacist.

6. Ensure that that those who administer the medicine know how to administer the medicine correctly so that this will deliver the correct dose. Ensure there is access to appropriate measuring devices. Consider providing written information.

7. Ensure that those who administer the medicine know how to store the oral liquid correctly and, if appropriate, to shake well before use.

8. Set up a system for reporting all errors (including near misses) and problems associated with compounding. This will help to monitor quality and identify problem formulations to prioritise risk management. The Pharmacovigilance centre is the ideal agency to collect this information.

In conclusion, compounding oral liquids for children is associated with a number of risks that can cause harm. If pharmacists, other health professionals and patients recognise these risks adverse events can be prevented.

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