

***Assessment of the accuracy of preparation and the stability of pediatric amoxicillin suspensions-
ablending of the pharmaceutical sciences with
clinical pharmacy***

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In pediatric practice in Kuwait, amoxicillin (trihydrate) oral suspension (Hiconcil^R) maybe dispensed. In most pharmacy practices, it is prepared by dispersing the dry ingredients in a specified volume of water immediately before providing the prescription medicine to patients. However, at many Government clinics in Kuwait, pharmacists provide only the bottle containing the dry powder to patients. Thus, the responsibility of preparing the medicine is devolved to parents. We determined whether parents were given proper instructions about preparing and storing the suspension and how accurately they prepared the medicine. As parents used different types of water to prepare the medicine, we determined in the laboratory whether the type of water used in preparing the antibiotic suspension affected its stability.

Methods:

A questionnaire was prepared in Arabic. It was divided into three sections dealing with the preparation and administration of the medicine, its constitution and storage and the directions

supplied by the pharmacist, respectively. To validate it, interviewers families completed it, commented on its clarity of expression and provided feedback on any ambiguities.

A Shimadzu LC10 AD HPLC and SPD-M10AVP diode array detector were used to assay samples for ampicillin. Analyses were made on a ShimpackGLC-ODS column using acetonitrile/0.1 M ammonium acetate, pH 7.8, (ratio of 10:40, flow rate = 1.5 ml/min) as the mobile phase. Amoxicillin was monitored at 230 nm and had $R_t = 5.2$ min under the assay conditions. Freshly prepared amoxicillin (ex Sigma) was used as the standard preparation. The assay was accurate 98.5-100.2% recovery using spiked samples ($n = 10$); coefficient of variation was 2.4% and sensitivity was < 1.0 mcg/ml.

The degradation rate constants of amoxicillin solutions were determined in deionized, mineral (Raudatain^R) and filtered tap water at 40, 50 and 60°C. Stability studies on three bottles of amoxicillin suspension (Hiconcil^R) prepared with the same types of water were performed at 4,25 and 40°C.

Thirty prescriptions for pediatric amoxicillin suspension were identified randomly at five clinics operated by the Ministry of Public Health in Kuwait City. The purpose of study was carefully explained to parents and they were asked to participate. After obtaining their agreement to participate, three days after the prescription was filled, by appointment, two interviewers visited the parents at their home. Parents completed the questionnaire and a sample of the amoxicillin suspension was taken for analysis. Samples were transported immediately to the laboratory and the amount of amoxicillin they contained determined by HPLC. Data from the Questionnaires were tabulated.

Results and Discussion:

The British Pharmacopoeia (1993) specifies that amoxicillin oral suspension shall contain "when freshly constituted not more than 120.0% of the prescribed or stated amount".

Also, "when stored at the temperature and for the period stated on the label during which the Oral Suspension may be expected to be satisfactory for use, not less than 80% of the prescribed or stated amount". The manufacturer states that Hiconcil^R should be stable for 14 days if stored at 4^oC and 7 days if stored at 25^oC. Seven of the samples obtained at interview three days after the prescription was dispensed contained < 200.0mg amoxicillin in 5ml and fell below the lower limit. As samples were obtained presumably three days after the medicine was prepared, this was likely due to errors in adding the water to make the suspension.

Data from the questionnaires revealed that most parents (22/30) used filtered tap water to prepare their suspensions. The Bp (1993) specifies that "Water" be used to prepare the suspension. "Water" is defined as "potable water freshly drawn direct from the public supply and suitable for drinking or freshly boiled and cooled Purified Water". Most water supplies in Kuwait do not meet the Bp (1993) specifications for "potable water" before or after filtration. We compared the degradation rates of amoxicillin solutions in de-ionized, mineral and filtrate tap water. The findings revealed the following order of degradation rates: filtered tap > > mineral = deionized water. For the Hiconcil^R suspensions. t_{90} at 25^oC was 3.6, 13.3 and 10.8 days for filtered tap, mineral and de-ionized water, respectively. Thus, storage of amoxicillin suspensions at room temperature after preparation with filtered tap water could result in failure to meet compendial standards. Moreover, patients could receive less than the prescribed dose, which possibly might result in failure of therapy.

An analysis of filtered tap water (ph=7.03) from the Health Sciences Centre using flame and furnace atomic absorption spectrometry yielded the following concentrations of elements (ppm) Ca: 66; Mg: 10; Zn: 0.8; Fe: 0.6; Cu: 0.3 and trace amounts, < 1 PPb, of Mn and Se. This water is likely better than water in most homes in Kuwait but certainly does not meet BP (1993) standards for water!

23/30 patients reported that they had received no direction from the pharmacist about preparing the suspension, and 13/30 parents reported storing the antibiotic preparation at room temperature, not in refrigerator. These findings showed that pharmacists did not provide adequate counseling to parents about the preparation and storage of the medicine.

Conclusion:

The practice of dispensing amoxicillin as a dry powder for parents to prepare antibiotic suspensions should be discontinued-almost one quarter of parents failed to prepare the suspension to compendial standards. The suspension should be prepared in the pharmacy using de-ionized or distilled water (Purified Water BP) before the medicine is given to parents. Pharmacists must counsel parents about the proper use and storage of the antibiotic suspension.

This study illustrates that one can incorporate expertise in the pharmaceutical sciences into a practice-based research project and improve patient care.

Acknowledgements:

We wish to thank the students in the Pharmacy Technician Class of 97 at the College of Health Sciences, PAAET, for their able assistance with the interviews and sample collections.

References:

1. British Pharmacopoeia (1993) Amoxycillin Oral Suspension. p. 774.
2. British Pharmacopoeia (1993) Water, p. 8.

