P P - 0 0 8 -"IMPLEMENTING APPROPRIATE COMPOUNDED PEDIATRIC MIDAZOLAM 3mg/ml SYRUP IN THE CLINICAL HOSPITAL BITOLA"

T. Dimitrovska Manojlovik,[1] D. Trombeva [2]

1.Clinical hospital-Bitola, Hospital pharmacy-Drug Information centre, Bitola, R. Macedonia,
2.Clinical hospital-Bitola, Control and analytical laboratory at the Department for infusion solutions production, Bitola, R. Macedonia,

CLINICAL HOSPITAL BITOLA

- **BACKGROUND:**

Prior to an operation or other invasive medical procedures, patients, especially children, experience a high degree of fear, stress and internal tension.Therefore introduction of preoperative drug administration (premedication) is intended to reduce these stresses through anxiolytic and sedative effects.The demand for such a medication has rised from the anesthezioligists in our hospital since supplying and registration of Midazolam HCl syrup has been discountinued.By that reason we approached of compounding and developing appropriate pediatric dosage form containing Midazolam HCl-syrup.

- **PURPOSE:**

To develop appropriate and stabile Midazolam 3 mg/ml syrup for preprocedural sedation and anxiolysis in pediatric patients.

- **METHODS:**

Three series of Midazolam 3 mg/ml syrup were prepared.The syrups were packed and stored (at the room temperature (cca. 25°C) in 100 ml light-resistant glass bottles.Prior of the dispensing of the preparations to the Department of Anesthesia, Reanimation and Intensive Care, quantitative analysis (Chemical tests and assays, USP 31.Ed) of the midazolam HCl content was done.After the analysis a half of the prepared quantity was dispensed to the prior mentioned department and the rest were kept in a dark place at room temeperature (cca. 25°C) in our pharmacy for indefinite period (we are still keeping them for further examinations).Test samples were taken periodically and in the same time from the dispensed and used preparations on the ward and from (in the pharmacy) kept preparations, and quantitative analysis of the midazolam HCl content was performed.Ingredients used for compounding of this drug were:Midazolam injectable sol. 5 mg/ml, vials of 10 ml (Panpharma, Fourgeres, France), Saccharosum (Alkaloid Ad, R.Macedonia), Aetherolleum cariophylli (Mediplant, Thessaloniki, Greece) and Aqua sterillisata (Department for infusion solutions production, in our hospital Ph.Eur). Determination (according USP 31.Ed; Chemical tests and assays) of midazolam HCl content as well as the testing of the physical properties-colour and odour (visual examination) were done at the Control and analytical laboratory at the Department for infusion solutions production in our hospital.

- **RESULTS:**

Quantitative examinations of midazolam HCl in the series of samples on the same day of the production indicated that the average content of the active substance was higher than 99,80% i.e. in the rank of declared concentrations.The average concentrations in all test samples after 1 month(30 days) and 2 months(60 days) of keeping or/and using (on the wards) were higher than 95% of initial midazolam HCl concentrations.This indicates no significant loss (degradation) of midazolam HCl.The concentrations of midazolam HCl started to decrease under 95 % of the initial, after 68th day of production date, so we withdrawed the prior dispensed (at wards) bottles at once.There was no presence of visible particles in none of the test samples, nor changes of colour and/or odour in the none of the test samples after 30, 60 and 90 days.The day of dropping of the midazolam HCl concentration below of the 95% of initial was a main criterium for expiry date decision.

- **CONCLUSIONS:**

In the hospital pharmacy of the Clinical hospital in Bitola, with restricted (for drug supply) budget, we formulated our own prescriptions and producing processes for Midazolam HCl 3 mg/ml syrup with expiry date of at least 60 days.Reinforcing the compounding process we solved many problems regarding drug supply in our hospital.For ensuring of the safe and effective use of this medicine we are obliged to continue with further control of the indicators for the product quality, that is a part of our next tasks.

- **REFERENCES:**

1. http://fagron.us/external/helpdesk_files/0000/0064/Stability_of_Midazolam_in_SyrSpend_SF_and_SyrSpend_SF_CherryJulAug2013.pdf
2. http://www.sickkids.ca/Pharmacy/Compounding-Service/
3. Martindale The complete drug reference, 34th Ed. PhP, London, Chicago, 2005
4. Remington's Pharmaceutical Sciences, 17th Edition. Mack Publishing Co., Easton, PA, 1985
5. www. Compounding Today. com
6. USP 31, The United States Pharmacopeial Convevtion 12601 Twinbrook Parkway, Rockville, MD 20852, may 2008
7. Ph. Eu. 3rd Ed, PhP, 1998
6. Pharmaceutical Dosage Forms and Drug Delivery Systems by Howard C. Ansel, Lippincott Williams & Wilkins, oct. 1999
7. Merck Index, 12th Edition, 1996 for solubility information
8. Handbook of Pharmaceutical Excipients, 4th edition, 2003
9. http://www.rphworld.com/link-65.html
10. Our own longlasting professional working experience.