"READY-TO-USE" INTRAVENOUS VANCOMYCIN TO AVOID DILUTION ERRORS IN THE NEONATAL INTENSIVE CARE UNIT (NICU): CHEMICAL STABILITY AND MICROBIOLOGICAL POTENCY

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Background and Objective

Vancomycin is the drug of choice in NICU's when severe neonatal infection is suspected after day 3-4 of life[1]. The initial empirical therapy in this rapidly life threatening condition often associates an aminoglycoside to broaden the spectrum. When sepsis is suspected in the neonate, antibiotic treatment has to be initiated immediately. Commercially available vancomycin, targeted for adults, needs to be reconditioned for neonatal use. Prior to IV infusion, 500mg of sterile dry powder are reconstituted to produce a concentration of 100mg/ml. Based on dose regimens of 10-15 mg/kg[2] in the very low birth weight infant (<1500g) further dilutions are necessary to obtain a final strength of 5mg/ml. These dilution procedures are carried out at the moment when the staff is preoccupied by the patients vital conditions. Medical errors increase in such stress situations[3] and could lead to dangerous under or over dosage. Vancomycin toxicity is debated, but has been associated with lasting ototoxicity[4]. Multiple aseptic manipulations can also lead to bacterial contamination[5,6]. Ready-to-use low concentration vancomycin prepared in the pharmacy could reduce these risks. Immediate availability around the clock is mandatory. This study investigated its chemical stability and microbiological potency (MP), which are prime conditions for its clinical use.

Previously in the wards :

Stage 1: reconstitution of the lyophilised vancomycin (5 or 10ml syringe)
Stage 2: withdraw necessary quantity into a 1ml syringe
Stage 3: further dilute into a 10ml syringe
Stage 4: attach syringe to pump driver
Stage 5: choose the desired volume after purging the line

Photos: William Griffiths

"Ready to use":

Stage 1: attach the syringe to pump driver
Stage 2: choose the desired volume after purging the line

Methods

Solutions of vancomycin (Vancocin®, E. Lilly) in Glucose 5% and NaCl 0.9% (50mg/10ml) were filled under aseptic conditions into 10ml polypropylene syringes (Plastipak® Becton Dickinson) and stored at 4°C and 25°C. Samples were analysed at T0, 1, 2, 4, 7, 14, 28, 42, 56, 98, 112, and 140 days. The microbiological assay was carried out according to the European Pharmacopoeia 2002 and the 6th Swiss Pharmacopoeia for the statistical analysis. The chemical stability was determined using HPLC[7].

The standards were the T0 solutions kept at -70° C and also the Vancomycin Reference (VRS). After 56 days at 4°C samples were placed at 25°C and analysed after 48 hours to simulate ward conditions (SWC).

HPLC Parameters

Merck Hitachi System with high pressure pump L-600 and D6000 interface.

Column:	Lichrospher 100 RP18 (5microns) 125/4/8mm.
Mobile Phase:	Triethylamine buffer Acetonitrile R Tetrahydrofurane 900:9O:10.
Flow rate:	1,5ml/min.
Injection Volume:	20 µl
Detection:	UV 280 nm
Internal standard:	Cephazolin Na (Kefzol® E. Lilly).
VRS :	RS0271 (E. Lilly)

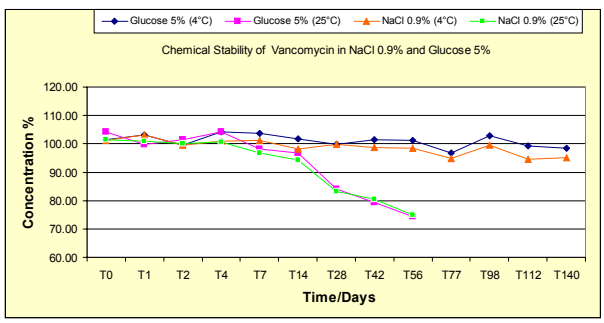
MP Parameters

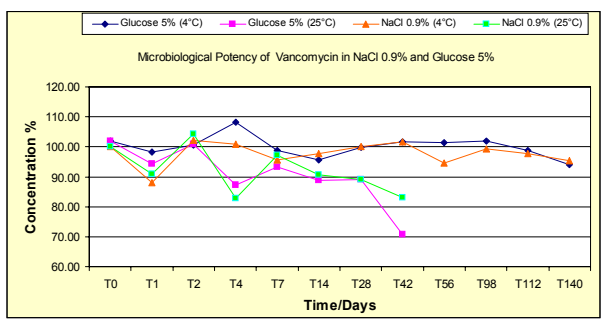
Method:	European Pharmacopoeia. 2002,
Assay:	Diffusion.
Micro-organism:	Bacillus subtilis spores
Culture Medium:	Antibiotic No 1
Buffer:	pH 8 for Vancomycin
Sample:	10 µl
Discs:	Non impregnated, diameter 6 mm BioMerieux 54991.
Incubation:	37-39°C

Reference Standard : T0 (kept at -70°C)

Results

Vancomycin is chemically stable in Glucose 5% and NaCl 0.9% after 140 days when stored at 4°C and its MP remains intact. Important losses are already seen after only 4 days at 25°C in both cases. The results using the two methods develop in an identical manner. The SWC samples were stable. Analysis will be continued until signs of chemical degradation and/or loss of MP is seen.





Conclusions

Syringes of "ready to use" low dose vancomycin, manufactured and supplied by the pharmacy in sterile sachets, can be stored in the NICU refrigerator for 140 days. They can be used in emergency situations, thus avoiding the danger of dilution errors and bacterial contamination without delaying the onset of the treatment. Once brought to 25°C, the solution must be used within 48 hours. This approach will be applied to other high risk products used in the NICU.

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Possible conflict of interest : nothing to disclose