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CDR-II – Lecture Notes - Cytotoxic Drug Reconstitution Procedure and Safety

Principle of safety during CDR preparation

1) Education and training of personnel

Training in drug preparation procedures should be undertaken prior to commencement of duties and when new equipment is introduced or procedures changed. Education and training of health professionals in cytotoxic drug preparation and handling is recommended to ensure that safe work practices are understood, developed, implemented and maintained.

2) Control of the working environment

Personal Protective Equipment should be worn by personnel. Attention to occupationally related work practice will maximize efficiency and productivity and minimize operator errors.

3) Adoption of safe working procedure

Follow the steps and guideline on working procedure. Drugs and its storage area and equipment need to be identified. Intravenous equipment and devices containing cytotoxic drugs should be clearly labelled with a permanent, adhesive and recognizable cytotoxic drug label.

Reconstitution and Preparation

Laminar air flow hood

Principle: Have a constant flow of of HEPA filtered air at a rate of approx 90 linear feet (6 feet tall) physically sweeps the work area and prevents the entry of contaminated air.

Wokspace of the hood used to prevent the contamination of compounded sterile products and parenteral preparations.

HEPA Filter

Principle: Removes 99.97% of all air particles 0.3mm or longer.

The Space between the HEPA filter and sterile product being prepared is known as the critical work surface. Air flow pattern is uni-directional. Filtration system consist of prefilter and HEPA filter.

Ensuring Proper air flow: Place products equidistance from the front and back of the laminar airflow to reduce the contamination.Before use, all interior of the laminar flow hood should be cleaned from back to front away from filter using 4x4 gauze with sterile water to irrigate it and next clean using 4x4 gauze – with isopropyl alcohol as disinfect from contamination.

Preparation Method

Step A : Performed in class 11 Type A or Type B laminar flow biological safety cabinet. The cabinet echaust should be discharged to the outdoors inorder to eliminate the exposure of personnel to drugs that may volatize after retention on filters of the cabinet. The work surface of the safety cabinet should be covered with plastic- backed absorbent paper. This will reduce the potential for dispersion of droplets and spills and facilitate cleanup.At the end of the work the paper is removed.

Step B: Personnel should wear long sleeved coverall of impermeable material, e.g. made from bonded Polyethylene fibre with a closed front and elasticized cuff, with suitable head protection

- overshoes of a similar impermeable material
- suitable respiratory protection
- long PVC, surgical latex, or purpose manufactured gloves

Step C : Chemotherapy Dispensing technique: Connect small gauge needle and 0.22 micron hydrophobic filter and close with the needle cap.

Step D: Disinfect the rubber stoppers of the diulent vial using 70% alcohol using cotton swab. Using needle punture the centre of the rubber stopper held at a 45º angle, then bring the needle upright to a 90° angle (this called straight slit cut technique) draw the diluent and kept close the needle with cap.

Step E: Disinfect the rubber stoppers of the drug vial using 70% alcohol using cotton swab. Insert the syringe to the drug vial which is filled with diluent at the centre of the rubber stopper.Slowly inject the diluent into the drug vial. Use a careful rotating motions to dislodge any powder from the inside surfaces of the vial. Finally keep the final product vial must be kept on the work surface to maintain stability hence it reduces the probability of spraying and spillage.

Step F: Use a 5 micron filter needle to draw the drug solution.

Step G : Syringes and IV bottles containing cytotoxic drugs should be labelled and dated. Before these items leave the prepararion area, an additional label reading, "*Caution chemotherapy, Dispose of properly*" is recommended.

Step H: After completing the drug preparation process, wipe down the interior of the safety cabinet with water (for injection and irrigation) followed by 70% alcohol using disposable events.

Step I: Contaminated needles and materials must be packed in a non resistant container along with any contaminated items and placed in a box labeled.

Step J: Hands should be washed between glove changes and after glove removal.

Step K: Cytotoxic drug wastes are categorized as regulated wastes hence it must be well packed based on the regulations and should be disposed according to national, state and local requirements.

Occupational Hazards Monitoring:

Many tests were employed to monitor health care workers' exposure to cytotoxic agents:-

1) *Urinary Mutagenicity*: Concentrated urine is usually tested with a bacterial mutagenicity assay (Ames test) that is sensitive to many of the cytotoxic drugs and/or their metabolites and the results compared to a control. The large percentage of the drug becomes mutagenic to the body.
2) *Chromosomal Aberrations*: Chromosomal aberrations represent damage to DNA that is visible in stained cells. Usually, the lymphocytes of nurses and pharmacists handling cytotoxic drugs are observed, increase in chromosomal damage.
3) *Sister Chromatid Exchanges*: Although Sister Chromatid Exchanges (SCEs) are typically measured in lymphocytes, similar to chromosomal aberrations and micronuclei, they are involved with DNA repair.

4) *Micronuclei Induction*: Micronuclei induction results from exposure to many chemicals that react with DNA and to determine the ability of a chemical agent to damage DNA resulting in the formation of small fragments of DNA termed micronuclei. Micronuclei are usually measured in peripheral lymphocytes, but also can be evaluated in other cell types.

5) *Urinary excretion of cytotoxic drug:* Direct measurement of antineoplastic agents and their metabolites in the urine of exposed workers by analytical methods. Can be analyzed by gas chromatography/mass spectrometry (GC-MS or GC-MS-MS), high performance liquid chromatography (LC-MS or LC-MS-MS) or high performance liquid chromatography with UV detection LC-UV.

Equipment maintenance

An effective equipment maintenance schedule should incorporate the following:

- inspection of cytotoxic drug safety cabinets, isolators and High Efficiency Particulate Air (HEPA) filters

- at regular intervals (a minimum of every 12 months)
- after relocation or mechanical/electrical maintenance
- keeping test records and a summary of results in a place accessible to employees
- Do not use a cabinet that has failed, until the fault has been rectified and the cabinet recertified
- performing microbial and air-particle testing routinely, and recording the results.

Chapter – 1 TPN Solved calculations

Provide TPN for a 75 year old female patient, who is 5 feet 2 in (ht), 120 lb (wt). Patient is confined to bed but no stress factors. The patient's laboratory records and based on experience decides to prepare a 2000ml TPN, utilising a 10% aminoacid injection as the protein, D50W as the dextrose source and a 20% lipid emulsion as the fat source with a satndard mixture of electrolytes, Minerals, Vitamins.Perform a basic calculations.

I. Weight 120lb=54.5kg
BEE (Total cal.req) Harris Benedict equation:-
Therefore 655 + (9.56 x wt) + 1.85 x height) - (4.7 x age)
655 + (9.56 x 54.5 kg) + (1.85 x 157.5) – (4.7x75)
= 655 + 521 + 291 – 352.5 = **1114.5 kcal/day**

II. No stress factor, therefore consider normal activity factor as 1.2
1114.5x1.2 = **1337.4 k cal/day**

III. Protein (required in grams):
54.5 x 0.8g/kg
= **43.6** gms/day

IV. The 10% aminoacid injection would require ;
$\frac{100ml}{10g}$ x 43.6 = **436 ml** of injection (AA)

V. Cal: Lipid in kcal
1337.4 k cal/day x 35%
= **467.95**

VI. Lipids in (grams)
$= \frac{467.95}{1\ day} \times \frac{1g}{40kcal}$

= **11.69 g/day**

VII. D50W as the (source of dextrose)
Basic Step:
1337.4 (kcal) – 467.95 kcal = 869.45
$= \frac{869.45}{1\ day} \times \frac{1gram}{3.4\ kcal}$
= **255.7 g/day**

D50W= 50g dex/100ml

$= \frac{100\ ml}{50g} \times 255.7$

= **511.4** ml D50W

VIII. Fluid Requirement:

a) if 120 lb x $\frac{1\ kg}{2.2\ lb} \times \frac{30ml}{1kg/day}$ = **1636.36 ml/day**

b) $\frac{1337.4}{1\ day} \times \frac{1ml}{1kcal}$ = **1337.4 ml/day**

Hence, in this case have given the predetermined value of 2000 ml of fluid requirement .the patient should receive 43.6 gms of protein, 436 ml of AA, 11.69 gms of lipids/day and 1337.4 ml to 1636.36 ml of fluid require per day.

Note: If aminoacid is given in the form of injection, follow the forth step and no need of calculating protein kilocalorie. And in the case if aminoacid injection is not used then please follow the regular steps.

Tutorial Questions

Discuss in detail on the aspetic technique involved in cytotoxic preparations.

Write note on the advantages of wearing personnel protective wearing equipment

Explain the planned maintenance schedule for the aseptic cabinet.

Explain the disposal methods of cytotoxic wastes.

Enumerate the complications of total parenteral nutrition.