Radiopharmaceutical Therapy: Agent/Protocol-Specific Procedure

I-131 meta-iodobenzylguanidine (Iobenguane Sulfate) (MIBG)

AN OPEN LABEL, EXPANDED ACCESS PROTOCOL USING I-131 METAIODO-BENZYLGUANIDINE (^{131}I-MIBG, Draximage®, IND # 76,227) THERAPY IN PATIENTS WITH REFRACTORY NEUROBLASTOMA, PHEOCHROMOCYTOMA, OR PARAGANGLIOMA

Radiopharmaceutical Agent:

I-131 Iobenguane Sulfate is a clear liquid for IV infusion. I-131 labeled meta-iodobenzylguanidine (^{131}I-MIBG) is a functioning analogue of norepinephrine taken up by sympathetic neurons and certain tumors. It is a highly specific radiopharmaceutical agent for the diagnosis and treatment of neuroblastoma and pheochromocytoma. I-131 decays by both beta and gamma emission and has a physical half-life of 8.04 days.

Drug Information Source:

Iobenguane Sulfate injection, labeled with either I-131 or I-123, is indicated as an adjunctive diagnostic agent in the localization of primary or metastatic pheochromocytomas and neuroblastomas. MIBG, when radiolabeled with larger amounts of I-131, has proven to be an effective therapeutic agent for children with relapsed neuroblastoma. It is currently being studied in combination with chemotherapy, which serves as a radiosensitizer. For additional information regarding this agent, consult MicroMedex or other standard references.

Administration/Treatment Schedule:

Prior to the patients' admission, Radiation Safety will coordinate the preparation of the the MIBG treatment room (see Addendum #6). A portable lead shield will be placed in the room and situated between the patients' bed and the door. A radiation monitor will be mounted in the cabinet at the head of the bed. A urine pump and tubing set will be brought into the room and drain directly into the patients' toilet. The tubing will be taped to the floor and connected to the patients' urinary catheter on the day of ^{131}I-MIBG treatment. Disposal containers for waste and soiled linen will be placed in the MIBG room and removed by Medical Physics/Radiation Oncology/Radiation Safety after the patient is discharged from radiation isolation. Protective clothing (gowns, gloves and shoe covers) will be placed in the anteroom. Pocket dosimeters, a stationary radiation detector (to monitor for contamination upon leaving the MIBG room), and a radiation Log Book will be placed in the anteroom. Patients will be admitted to the American Family Children's Hospital on the day prior to the scheduled ^{131}I-MIBG therapy. Thyroid blockade will be started 8 - 12 hours before the scheduled treatment. SSKI solution (1g/ml, 1 drop = 50 mg) will be administered in a loading dose of 6 mg/kg p.o. 8 -12 hours prior to the MIBG injection, then be given at 1 mg/kg/dose q 4h days 1 - 7, then 1 mg/kg/day through day 45 post injection.

Each patient will have a urinary catheter inserted on the morning of the MIBG infusion. A Percutaneous Intravenous Central Catheter will also be inserted if the patient does not already have a central venous catheter. Both procedures will be performed in the Pediatric Sedation clinic. The urinary catheter will be kept in place for a minimum of 72 hours, or until the patient is released from radiation isolation if incontinent. The catheter will prevent accumulations of large amounts of radioactivity in the bladder. Urine will be pumped directly into the toilet. The pump will be turned on every 4 hours by the caregiver and run for 15 minutes. The toilet will be flushed 5 times after each pump operation. A spare pump will be available in the event of a pump malfunction. In the event of a toilet malfunction, the urine will be diverted to drain into the sink in the patient's bathroom. Intravenous fluids will be administered at 125 ml/m^2/hour to maintain adequate urine output.

If the Foley malfunctions or becomes dislodged, the RN is to notify the attending physician (pediatric oncologist) and medical physics/radiation oncology/radiation safety personnel immediately. If the Foley needs to be flushed or reinserted, the RN will perform these tasks.

Other waste products (e.g., feces, emesis) will be emptied into the toilet by the caregiver and the toilet flushed 5 times.

Patients will be connected to a cardiac monitor and blood pressure cuff prior to the ^{131}I-MIBG infusion. Vital signs will be monitored remotely every 15 minutes during the ^{131}I-MIBG infusion by the nursing staff. Thereafter, vital signs will be checked once a day unless the patient becomes unstable.

No medications with potential interference with MIBG uptake may be administered (see addendum #32). Medications will be reviewed by the mIBG Therapy team.

Dose will arrive at the hospital via Fed-Ex (or courier) by 10:00am on day of treatment. The Nuclear Pharmacist will communicate with the supervising nurse practitioner verifying the dose has arrived and to verify that the patient has arrived, and the treatment is still scheduled to proceed. Target time for patient administration is 13:00.

Dose Range:

The dose of ^{131}I-MIBG will be ordered in mCi/kg and be dependent on the research protocol.

The Nuclear Pharmacist will dispense the prescribed dose of ^{131}I-MIBG. A Nuclear Medicine Technologist transport the dose to the MIBG treatment room on P4 and will initiate the ^{131}I-MIBG infusion utilizing a syringe pump. The ^{131}I-MIBG will be infused over 90 - 120 minutes through a central venous catheter or PICC line, followed by a 30 ml normal saline flush. The infusion apparatus will be checked for leakage after 20 minutes from the start of the infusion and periodically throughout the infusion by the Nuclear Medicine Technologist, Authorized User Physician, or Nuclear Pharmacist. In the event of a leak the pump is stopped by the Nuclear Medicine Technologist, and the following individuals will be notified.

Nuclear Medicine MD
Radiation Safety
Nuclear Pharmacist
Ken DeSantes or Neha Patel

A sheet with emergency contact information will be posted in the anteroom.

After completing the ^{131}I-MIBG infusion, the Nuclear Medicine Technologist will disconnect and dispose of the tubing used for ^{131}I-MIBG administration and reconnect the standard IV tubing. The nursing staff will re-initiate the patient's IV fluids.

Necessary Training:

All hospital personnel caring for patients receiving ^{131}I-MIBG therapy will be required to complete an initial radiation safety training course, as well as an annual refresher course. Nurses will receive additional training in procedures related to taking care of ^{131}I-MIBG patients by the, P4 Clinical Nurse Specialist and/or the Pediatric Oncology Nurse Practitioner prior to each ^{131}I-MIBG treatment. Parent/Caregiver training is outlined in addendum #15. All PICU RN's and MD's, as well as RT's will receive education related to caring for MIBG patients and radiation safety. Any other staff that need to enter the room on an unanticipated basis will be trained at the time they are needed.

Written Directive and Validation:

Once a patient has been identified, the Pediatric Oncology staff will call the Nuclear Pharmacist to determine treatment dates, as well as verify the availability of the drug. Pediatric Oncology support staff will deliver the pre-signed physician orders to Nuclear Pharmacy. Order sets will include the patient weight. The Nuclear Pharmacist will hand deliver the order set to the Nuclear Medicine physician (Authorized User), who upon approving the therapy, will complete and sign the written directive portion of the Radionuclide therapy dose documentation form and return it with the orders to the Nuclear Pharmacist, who will then place the order set in the designated slot In Room E1/378. If the treating Nuclear Medicine physician is unavailable, the order set will be forwarded to the Nuclear Medicine faculty physician of that day. The Nuclear Pharmacist will verify the written directive, prepare the Radiopharmaceutical Requisition Form, and order the dose. After the dose is ordered, Nuclear Pharmacy staff will retain the original documents until the day of administration.

Ordering Procedures: The original physician order set and the signed ^{131}I-MIBG dose documentation therapy form must be received by the Nuclear Pharmacist by 12:00 noon on the Tuesday before the planned therapy. The Nuclear Pharmacist will order the dose as soon as all documentation is received and signed by the designated Authorized User.

Drug Procurement/Preparation: The Nuclear Pharmacist will order the radiopharmaceutical after receiving the completed Radionuclide Therapy Form. Upon receipt of the radiopharmaceutical and verification of patient arrival, the product will be thawed. The prescribed dose will be drawn up in a 60mL syringe to within 10% of the prescribed range, with the dose being verified by the administering Nuclear Medicine Technologist and documented on the Radionuclide Therapy Dose Form. The syringe will be labeled and placed in the shielded syringe pump along with the saline primed extension tubing. The pump will be placed on the designated shielded cart and will remain in the Nuclear Pharmacy until the ^{131}I-MIBG is ready to be administered.

Pharmacy Product Validation: Before release to the patient, the ^{131}I-MIBG will be tested for to ensure the 90% or greater I-131 is bound to the MIBG.

Materials: Waters Accell Plus CM Sep-Pac, Ethanol, Sterile water, 10 ml test tubes.

Procedure

1. Using a Waters Accell Plus CM SepPac cartridge, wet the sepPac with 5 ml ethanol. The long tip of the SepPac must be connected to the flushes
2. Rinse with 5 ml sterile water
3. Add 1/20 ml MIBG to SepPac. Dilute to around 0.5 uCi
4. Flush SepPac with 5 ml sterile water into a 10 ml test tube (flush tube)
5. Place cartridge into a second 10 ml test tube (A)
6. Place the cartridge tube into a well counter and record (A), set counter on 131-I
7. Count both tubes (A and flush) in the well counter, add counts together and record (B), set counter on 131-I
8. (A/A+B x 100 = % tagged. Must be greater than 95% - compare to TLC. Comments: Procedure must be performed immediately after the dose defrosts. Results of bound iodine should be greater than 90%.
   Record results on worksheet.
   Contact physicians if there is an aberrant or low result.

Parent/Caregiver Instructions/
Education Validation: Parents/caregivers will receive radiation safety training on the day of their initial consultation, in addition to receiving written material describing the procedures for caring for an ^{131}I-MIBG patient. Reference material will also be available on-line. Refresher training will be provided to parents/caregivers by medical physics/radiation oncology/radiation safety

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