
Criteria for Determining Optimal Pediatric Dosage for a Diagnostic Nuclear Medicine Procedure

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Objective: The purpose of this paper is to provide information on the technical issues that must be addressed when adapting radiopharmaceuticals for use in children and to review the criteria and formulas currently used to calculate pediatric radiopharmaceutical dosages.

Methods: We conducted a phone survey of the nation's top medical facilities for pediatric care to find the criteria employed to establish radiopharmaceutical dosing guidelines for children. Technical pediatric dosing considerations were also obtained from the medical literature.

Results: The majority of institutions surveyed use body weight as the sole criteria in the determination of pediatric dose and empirically derive their minimum allowable activity limits. Adult dosages, established at 70 kg, are used as the maximum allowable activity limits.

Conclusions: Although the medical literature supports the use of body surface area as one of the most reliable methods of calculating pediatric radiopharmaceutical dose, the majority of top pediatric health care facilities prefer to use body weight as the only variable in the calculation of optimal pediatric dosage. Given the importance of issues that must be considered to ensure the radiation safety and the physical and mental comfort of the child, we believe that all pediatric radiopharmaceutical dosing guidelines and considerations warrant further attention.

Key Words: pediatric dosage; ALARA; body weight; body surface area; minimum and maximum allowable activity

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Many methods to calculate optimal pediatric radiopharmaceutical dosages have been proposed by researchers in their attempts to compensate for the altered, and often unpredictable, physiologic responses in children. These methods have also attempted to preserve the diagnostic integrity of nuclear medicine procedures while maintaining the principle of as low as reasonably achievable (ALARA). However, other technical considerations including the type of imaging equipment and

procedure, energy of radionuclide, effective half-life of the radiopharmaceutical and the percent of localization in the organ of interest also need to be recognized. At present, the majority of the medical literature supports body weight and body surface area as the most rational criteria to use in the calculation of optimal dosages for pediatric patients, although the establishment of minimum and maximum allowable activity guidelines remains subjective and must be empirically derived.

Radiopharmaceuticals have an established function within the diagnosis and management of various pathological conditions in children. However, the application of ionizing radiation in children is a complex issue that deserves the consideration of many factors. The most important issue to consider is the radiosensitivity of the child, which makes it of utmost importance to adhere to the principle of ALARA. This principle states that every reasonable effort should be made to maintain radiation exposures at the lowest possible levels. Therefore, the administration of any amount of a radiopharmaceutical beyond what is essential to obtain a useful nuclear medicine study should be avoided. Children have a long life expectancy and an entire reproductive future ahead of them, and they are unable to provide informed consent, which makes it our ethical obligation to significantly reduce the radiation burden to their rapidly developing organ systems whenever possible.

There are many other aspects of pediatric radiopharmaceutical application that are deserving of our attention, such as the use of proper injection and immobilization techniques. It is especially necessary to develop proper immobilization techniques because of the patient movement encountered in almost all pediatric nuclear medicine studies. Frequently, radiopharmaceutical dosages are increased which results in shorter image acquisition times. Although this has been an effective method of dealing with uncooperative patients, it also increases the child's radiation burden. Children may be sedated; however, the sedation of young children precipitates its own dangers and should be approached carefully with an appropriate monitoring protocol to ensure the maximum safety and recovery of the child (1). In addition to these concerns, there will be a gradual move by the Food and Drug Administration (Nguyen T, *personal communication*, December 1993) to

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TABLE 1
Pediatric Health Care Centers Surveyed

1. Children's Hospital, Boston, MA
2. Children's Hospital, Denver, CO
3. Children's Hospital Los Angeles, Los Angeles, CA
4. Children's Hospital Medical Center, Cincinnati, OH
5. Children's Hospital and Medical Center, Seattle, WA
6. Children's Hospital of Philadelphia, Philadelphia, PA
7. Children's Hospital of Pittsburgh, Pittsburgh, PA
8. Children's Memorial Hospital, Chicago, IL
9. Children's National Medical Center, Washington, DC
10. Columbia-Presbyterian Medical Center, New York, NY
11. Johns Hopkins Hospital, Baltimore, MD
12. Miami Children's Hospital, Miami, FL
13. Stanford University Medical Center, Stanford, CA
14. St. Louis Children's Hospital, St. Louis, MO
15. St. Jude Children's Research Hospital, Memphis, TN
16. Texas Children's Hospital, Houston, TX
17. UCLA Medical Center, Los Angeles, CA
18. University of California San Francisco Medical Center, San Francisco, CA
19. University Hospitals of Cleveland (Rainbow Babies and Children's Hospital), Cleveland, OH

require drug manufacturers to provide pediatric radiopharmaceutical dosing recommendations for more of their products. At present, there are only four radiopharmaceutical cold kits, macroaggregated albumin (MAA)¹ (2-5), sulfur colloid (7-9), oxidronate (HDP) (10), and mertiatide (MAG3®) (11) that contain limited recommendations for pediatric use. The complexity of pediatric dosing considerations, combined with the absence or insufficiency of manufacturers dosing guidelines, has prompted us to examine this subject further through a survey of the nation's top pediatric care facilities and a review of existing medical literature.

MATERIALS AND METHODS

For the past six years, *U.S. News & World Report* has attempted to rank the nation's top medical facilities. At the time of our survey in 1994, the top 19 medical facilities for pediatric care in the 1994 *U.S. News & World Report* survey were ranked solely on reputational scores, which were obtained through a survey of specialists from 1992 through 1994 (12).

We conducted a survey of these 19 institutions to find the criteria employed to establish optimal, minimum and maximum radiopharmaceutical dosing guidelines. A listing of the 19 institutions surveyed is given in Table 1. We spoke to supervisors of nuclear medicine departments, nuclear medicine physicians, chief nuclear medicine technologists and other nuclear medicine technologists directly involved with pediatric radiopharmaceutical administration to find the criteria used to establish optimum, minimum and maximum radiopharmaceuti-

¹ The package insert of TechnoScan® MAA, Mallinckrodt Medical, Inc., St. Louis, MO, is the only one among the five commercial MAA cold kits which states that the safety and effectiveness in pediatric use of technetium-99m-MAA has not been established (6).

TABLE 2
A List of the Telephone Survey Questions

1. What do you consider as valid criteria for the calculation of pediatric dose?
2. What method of adjusting radiopharmaceutical dosages for children does your hospital consider when establishing minimum and maximum administered activity limits? If no specific method is used, how were those minimum and maximum administered activity limits obtained?
3. If a pediatric patient dose is calculated but is too minimal to do an adequate scan, do you increase the dose? If you do increase the dose, what method of adjusting pediatric dosages do you use to calculate that increase?
4. What additional information do you feel is important?

cal dosing guidelines. A list of the questions that were asked of each subject surveyed is provided in Table 2.

RESULTS

Fourteen out of 19 medical centers identified for this survey responded for a response rate of 73.6%. Of those 14 facilities who responded, nine (64.2%) used body weight as the sole criteria for pediatric dose calculation, one (7.1%) center used body surface area (BSA) as the sole criteria, and four (28.5%) used body weight for the majority of dose calculations, relying upon BSA for some of their studies. Minimum allowable activity limits were empirically derived by 12 of 14 institutions (85.7%) and two (14.2%) respondents were unaware of how their minimum activity values were obtained. All 14 institutions (100%) established their maximum allowable activity limit at the adult dosage for the particular study, and administered the adult dosage to children weighing 70 kg or more.

DISCUSSION

The majority of pediatric health centers prefers to use body weight as the dominant criteria for adapting radiopharmaceutical dosages for children. However, this method is not entirely appropriate for all studies. Pediatric nuclear medicine studies and their technical requirements differ significantly from what is necessary for adults, making the calculation of radiopharmaceutical dosages difficult. From a physiologic perspective, children have known immature renal and hepatic systems and manifest variances in drug absorption, distribution, metabolism and excretion. These conditions, particularly in the very young child, may result in altered responses in the biological localization of trace elements and the mechanisms involved in the localization of labeled compounds (13). It is important to consider the ALARA principle, the imaging procedure desired (static vs. dynamic and/or limited vs. SPECT), the imaging equipment used, the energy of the radionuclide, the percent of localization in the organ of interest and the biologic half-life of the radiopharmaceutical (1). When considering the diversity of these issues, it becomes obvious that the use of only one method to calculate pediatric dose can never truly fulfill the

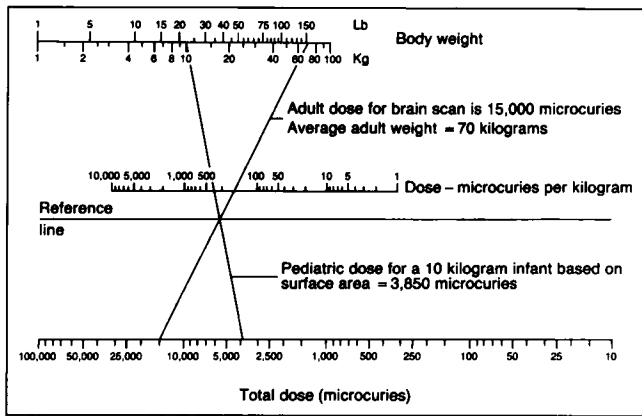


FIGURE 1. A modified chart of the Glazko's nomogram for pediatric dosages based upon body weight or body surface area.

different requirements of each criteria or nuclear medicine study.

Body Weight

While it is true that adjusting radiopharmaceutical dosage by pediatric body weight results in a slightly lower radiation exposure, quantifying the activity to be administered by body weight is more appropriate if the ratio of the weight of the organ of interest to total body weight does not vary with age (14). This is applicable to most organs, since body weight is closely correlated with the growth of many organ systems (15). A notable exception to this is the brain, which reaches its maturation weight at an early age (15). The use of body weight for dose calculation has also been recommended for use in the static imaging of thick organs (i.e., liver), since the most significant factor in study quality is information density (16). However, it is generally recognized that since the dose requirements per unit of body weight are higher for children than for adults, any radiopharmaceutical dosage adjusted solely by body weight may be inadequate for the examination. This method may also tend to produce dosages that are too small to be effective when dealing with children of extremely low body weight or too excessive in larger children.

Body Surface Area

BSA is very closely related to organ size, cardiac output, glomerular filtration rate, plasma volume, extracellular fluid volume and metabolic activity, which makes it an accurate method for pediatric radiopharmaceutical dosage adaptation for many nuclear medicine studies. It has been especially recommended for the static imaging of thin organs, such as the thyroid, where the information density is determined by the amount of activity in the organ divided by the imaged area (16). Since BSA is calculated in square meters, this method can also be very useful in determining radiopharmaceutical dosages in children who are not of average height or weight for their ages. To simplify the process of obtaining pediatric dosages from BSA, a nomogram developed by Glazko is often used. Figure 1 is a modification of this simplified conversion scale (13). However, the calculation of pediatric radiopharma-

ceutical dosage through the use of BSA is not without its disadvantages. As with body weight, calculating pediatric dosages with BSA can lead to an underestimation of the dosage at the low end of the scale, or an overestimation of the dosage at the upper end of the scale (1). Radiopharmaceutical dosage adjustment by BSA also results in slightly higher radiation exposure values for the child.

Minimum and Maximum Allowable Activity

The formulation of minimum and maximum allowable activity guidelines is an important aspect of pediatric radiopharmaceutical administration. Since adjusting pediatric dosages by body weight or BSA often leads to an underestimation of the administered dosage in very small patients, the establishment of a minimum allowable activity limit is required to ensure that no radiopharmaceutical is ever administered at a quantity below that which is diagnostic and, therefore, useful. The practice of dose reduction with respect to the ALARA principle is admirable, however, any benefits to be gained from decreasing the child's radiation exposure are rapidly lost if the procedure has to be repeated and another radiopharmaceutical dose given.

Maximum allowable activity limits are also necessary to restrict radiation exposure by establishing the greatest amount of a radiopharmaceutical dosage that should be given to a child to ensure the quality of the study without compromising the child's immediate or future radiobiological safety. Radiation safety is usually the biggest concern since most nonradioactive complexes are administered in subpharmacologic amounts.

CONCLUSION

The medical literature supports the use of BSA as the most accurate method by which to adapt radiopharmaceutical dosages for use in children. However, at this time the majority of the nation's top pediatric health care facilities (64.2%) use the child's body weight to adjust the administered activity. A small percentage (28.5%) of the institutions surveyed use both formulas, relying upon body weight to establish most of their pediatric radiopharmaceutical dosages and BSA in a limited number of studies. At this time, there is no direct method to assist in establishing minimum and maximum allowable activity limits, although most institutions have compensated for this lack of scientific data by developing their own minimum allowable activity parameters through empirical observations of radiopharmaceutical behavior in children. All institutions (100%) surveyed have currently set their maximum allowable activity limit at the adult dose established for the particular study involved, and administer this maximum limit for pediatric patients weighing 70 kg or more. The technical aspects of imaging and the spatial resolution needed for region of interest assignment make it imperative for us to choose a radiopharmaceutical dosage formula based upon the technical requirements deemed clinically necessary. Although there are aspects of pediatric radiopharmaceutical administration that warrant further attention to maximize the safety of all children, close attention to these factors will yield a significant reduction in unnecessary radiation exposure for children of all ages.

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