In Vivo

Modification of the Schilling Test for Pediatric Studies

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Distribution of [^{57}Co] cyanocobalamin was found to be quite inhomogeneous within the filler of dosing capsules from two manufacturers. Up to 6% of activity was found in or adhering to the capsule wall itself. A volumetric procedure for pediatric Schilling tests is described in which part of a capsule containing [^{57}Co] cyanocobalamin is administered.

A prime concern in the practice of nuclear medicine is to obtain the maximum information per study from the administration of the least possible radioactivity to the patient. This is especially true in the pediatric population. We describe previously unreported sources of error in performing the Schilling test (*1*) in children, and how the investigation of these problems led to modification of our protocol.

Previously in our laboratory the Schilling procedure involved counting a "standard" solution and comparing these counts to patients' urine sample counts. The standard solution was prepared by dissolving a [^{57}Co] cyanocobalamin capsule in a solution of constant volume, generally 125 ml, contained in a plastic counting bottle ([^{57}Co] cyanocobalamin adheres to glass). A capsule of the same lot number was administered to the patient. Even though manufacturers do not suggest dividing capsules, in our laboratory pediatric patients were given approximately half of a capsule in order to reduce whole body radiation exposure, which ranges from 54 mrad/μCi for a neonate to 9.1 mrad/μCi at age 10 (*2*). The capsule was opened and an estimated 50% of its contents were administered to the patient. The contents of the unadministered half were then dissolved in a container of constant volume. The net activity delivered to the patient was calculated by subtracting the residual counts from the counts in the standard solution.

On one occasion this technique resulted in a negative "net" standard value. Therefore, the half capsule *not* given to the patient contained more counts than the "standard" solution from another intact capsule! To be certain that one is reducing the radiation dose to the recipient of the capsule, one must determine the distribution of the radioactive material within that capsule. Otherwise one may give a half capsule on the assumption that the radioactivity to the patient is reduced by approximately 50%—only to find that the *entire* amount of [^{57}Co] cyanocobalamin was located in either the administered or the unadministered half. In order to further investigate this problem we analyzed the distribution of [^{57}Co] cyanocobalamin in the capsule filler and capsule wall.

We specifically investigated the following because they were not stated in the product information:

- degree of inhomogeneity of distribution of Co-57 within filler
- relative amount of Co-57 in both capsule wall and filler
- the coefficient of variation (CV) between individual batches of capsules from two manufacturers.

Materials and Methods

The contents of Co-57 capsules, 10 from Company "A" and 10 from Company "B", were investigated. First, each Co-57 capsule was prepared so that the distribution of activity within it could be individually determined. The Co-57 capsules were opened and the filler divided into halves. Consistently, the same first half (by color, shape, and weight) of the filler was placed in a plastic counting bottle with 125-ml water and counted for 10 min., typically yielding 600,000–1,000,000 counts. Then the other half of the capsule filler was added to the same Co-57 solution, and the solution was again counted for 10 min. In this way, percentages of counts from both halves of every capsule were obtained. To determine the activity present in the capsule wall, the solution containing the filler was recounted but because it had the capsule wall dissolved in it, this solution contained the entire Co-57 capsule. The previously obtained counts from both halves of the filler were subtracted from the counts of the entire capsule solution. This result represented the counts in the capsule

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wall. The final step involved counting a batch of ten unopened capsules from each company to determine the mean, standard deviation, and CV between batches. Student's t test on the difference between means of paired samples was then calculated for the appropriate comparisons.

An alternate method that had been proposed for dose reduction was to let the capsules decay for one half-life and then administer the total capsule. This method is not feasible because the shelf life is only 180 days, whereas the physical half life is 270 days. This means the capsule itself expires before it decays to 50% of initial activity.

Results

The average capsule of Company A contained 44% of the activity in the first half and 56% in the second half. The average Company B capsule contained 73% of the activity in the first half and 27% of the activity in the second half. These are significant differences (Table 1). However, for the A capsules 9 out of 10 had more activity in the *second* half of the capsule, while 8 out of 10 B capsules had more activity in the *first* half. Therefore the t value is higher for Company A. The half with maximum distribution was thus not always predictable. The CV for each half appears in Table 2. One parameter that relates to the overall uneveness of distribution within a capsule (independent of which half has the highest concentration) is the ratio of the mean of the magnitude of the difference between halves to the sum of the means of the halves. This parameter is 13% for Company A and 73% for Company B. (The larger the percentage, the more uneven the distribution is.)

From the counts obtained, the fraction of the total capsule activity found in the capsule wall was determined and appears in Table 3.

Finally the CV for the capsules from the two companies was examined. Within each batch there was no significant variation of activity/capsule. For Company A the CV was 0.4% and for B 1.3%.

TABLE 1. Mean Fractional Distribution of Activity Between Halves of Capsule.

	First Half*	Second Half	t	p
Company A	0.44	0.56	5.2	0.001
Company B	0.73	0.27	2.4	0.05

*Mean First Half / Mean First Half + Mean Second Half

TABLE 2. Coefficient of Variation of Each Half of Capsule.

	First Half	Second Half
Company A	8.3%	6.3%
Company B	41.8%	111.4%

TABLE 3. Capsule Wall Activity as Fraction of Total Capsule (Wall Plus Filler).

	Average	Range
Company A	3.8%	2.3-6.0%
Company B	2.7%	1.3-5.3%

Discussion

We have shown that A capsules distribute Co-57 B_{12} more evenly than B capsules, which exhibit considerable variation within each half. The p value for difference between the two halves is, however, smaller for Company A (more significant difference) because the same half had consistently different (higher or lower) activity—9 out of 10 times for A, only 8 out of 10 for B. Up to 6% of total activity may be in the capsule wall.

As a result of these findings, we discontinued the described Schilling test procedure. Our current method of performing the Schilling test in children is as follows:

The entire Co-57 capsule is dissolved in 125 ml of water in a plastic volumetric counting bottle and counted. A carefully measured fraction of this solution is administered to the patient depending on patient size and tolerance to the amount of solution ingested. Often the solution must be administered through a nasogastric tube. After the Co-57 solution has been put through the tube, it may be rinsed with an irrigation solution containing intrinsic factor if the Stage II test is to be done. Water is added to the remaining solution, again adjusting the volume to exactly 125 ml to insure identical counting geometry. This solution (and secondary container or nasogastric tube if used) is counted and subtracted from the initial count. This net result is the standard to be used for determining the percent of urinary excretion in the Schilling test. Since this standard is prepared and counted on the day activity is administered, it is necessary to include a factor accounting for radiation decay to the day when the 24- and 48-hr urine samples are counted. A 125-ml aliquot of each urine sample is counted. The formula is:

Percent dose in urine =

$$\frac{\text{net CPM specimen} \times \left(\frac{\text{total urine volume}}{125\ \text{ml}}\right)}{\text{net CPM of administered Co-57 std.} \times \text{decay factor}} \times 100.$$

We have found this method easy to perform, and it produces accurate results even in children weighing only 10 lb.

References

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