MIDAZOLAM-INDUCED AMNESIA:
A DOSE-RESPONSE STUDY IN FILIPINO ADULTS OF DIFFERENT AGE GROUPS

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ABSTRACT

This randomized double-blind controlled study determined the minimum dose of intravenous midazolam that caused anterograde amnesia in 50% of adult Filipino subjects of different age groups. It also determined the relationship between the required and actual doses of midazolam and the resultant amnesia with factors of weight, age, sex and duration of anesthesia as controls. A total of 150 patients scheduled for different surgeries and procedures were divided according to three age groups: A=20-39 yr, B=40-59 yr, and C=60-79 yr. The groups were further subdivided according to five midazolam dosages: 0.01, 0.02, 0.03, 0.04 and 0.05mg/kg. Colored geometric cards were shown to the patients before and three minutes after giving intravenous midazolam. Post-operatively, recall and recognition of the cards were assessed. Using Probit analysis, the ED50 values of midazolam for groups A, B and C were 0.023 mg/kg, 0.020 mg/kg and 0.017 mg/kg, respectively. Based on the results, the required dose seemed to be a better predictor of amnesia than the actual dose. Age, sex and to a lesser extent, the weight of the patient but not the duration of the procedure were found to influence resultant amnesia. Because of the possibility of gender influencing midazolam-induced amnesia, it is recommended that future studies be made among Filipino subjects using gender as a controlled variable. Other variables that should be considered are the level of anxiety and the level of sedation of the patients.

There are instances wherein an anesthesiologist is requested to only provide anxiolysis and amnesia to a patient under local or topical anesthesia. In doing so, the anesthesiologist tries to avoid over sedation and unnecessary movements. Furthermore, the anesthesiologist also tries to ensure that an anxious patient does not recall any undesirable event related to the procedure (e.g. performance of a retrobulbar block or the sound of instruments in the background). On other occasions, a difficult airway may only allow “awake” intubation. In these cases, drugs are carefully given so as not to cause sedation that can compromise the airway. There are also common anesthetic and surgical situations wherein “light” anesthesia combined with either local anesthesia or neuromuscular block may be the only regimen that can be safely tolerated by the patient (e.g. patients with debilitating disease, patients presenting for bronchoscopy and obstetrics). In these situations, anesthesiologists commonly use midazolam, a water-soluble benzodiazepine known for its anxiolytic and amnesic effects. A common practice in our institution is to give midazolam at a low dose of 0.5 to 1.5mg. However, amnesic responses are variable and anecdotal.

Literature Review

The amnesic properties of midazolam result from an impairment in explicit (conscious) acquisition of new material. This is likely mediated through the GABAA receptor complex, which contains the benzodiazepine receptor binding site. This GABAA receptor site is also believed to be the locus of the anxiolytic effect of the drug. Furthermore, recent research findings suggest that the anxiolytic and the amnesic properties of the benzodiazepines are functionally linked. Anterograde amnesia produced by midazolam is said to be dose related and often parallels the degree of sedation.

Nadin and Coulthard revealed that amnesia is more consistent when a higher dose (>5mg) is used and it is completely unreliable when given in lower doses. A study done by Kotilla and Tarkanne on 76 patients who underwent bronchoscopy revealed that a dose of 0.05 mg/kg of intravenous midazolam produces amnesia in 36% of patients and in 75% of patients when the dose is increased to 0.1 mg/kg. In a study over a duration of 2 years on 337 patients who underwent bronchoscopy, the mean dose of midazolam which produces light sleep and complete amnesia is 0.16 +/-0.095 mg/kg. Another study revealed
that a dose of 0.07 mg/kg produces insufficient amnesia whereas a dose between 0.10 mg/kg to 0.13 mg/kg causes adequate amnesia. A dose-finding study was conducted among elderly patients aged 60 to 86 years old using doses of 1.0, 2.0 and 3.0 mg of midazolam. Results of the study showed that all three doses of midazolam produce rapid onset of sedation, amnestic, and anterograde amnesia which were unrelated to body weight, age, or American Society of Anesthesiologists (ASA) physical status. These findings are supported in previous studies which showed that elderly patients require less midazolam for intravenous induction of anesthesia compared to young adults. A possible explanation for the aforementioned findings is the increased sensitivity of the central nervous system to the effects of midazolam with increasing age.

Among Filipinos, it is observed from experience that amnesia occurs at a dose between 1.0 to 2.0mg only. An average Filipino weighs between 45 to 55kg which corresponds to a possible amnesic dose of 0.02 to 0.04mg/kg - a dose range significantly lower than values observed in previous studies.

Relevance of the Study

Knowing the minimum dose that will render amnesia to 50% of the study population will be very critical when confronted with patients who can only tolerate very light sedation and those who will undergo procedures where amnesia is crucial and over sedation is detrimental. If Filipino subjects indeed have lower midazolam dose requirements for amnesia, knowing that critical dose will spell a lot of difference in the practice of anesthesia in the local setting.

There is also a common practice of presuming that a certain actual dose, (e.g. 1 mg) will render amnesia to most patients. However, this may not give reliable effects when applied to patients of different weights. A question then arises: Will a minimum dose requirement in mg/kg (required dose) therefore provide better reliability and predictability in terms of the resultant amnesia?

Objectives of the Study

1) To determine the minimum dose of intravenous midazolam that can cause anterograde amnesia in 50% of adult Filipino subjects of ages 20-39 years, 40-59 years and 60-79 years and;

2) To determine the relationship of the required and actual doses of midazolam and the resultant amnesia using factors of weight, age, sex, and duration of anesthesia as controls.

METHODOLOGY

This is a randomized, double-blind clinical trial conducted from March 2004 to August 2004 in a single medical institution. The sample size was calculated using the software Sample Size Table for Clinical Studies. Calculation was based on the expected mean dose difference of 0.6mg and a 0.05 level of significance and power of 80%. One hundred-fifty patients, aged 20-70 years old were included as they came for various elective surgeries or procedures. All of the patients were classified as either ASA I or II. They were not given any sedative pre-medications. Patients with a history of chronic use of benzodiazepines or drugs that affect the metabolism of benzodiazepines (i.e. erythromycin, azole antifungals, diltiazem, verapamil, cimetidine and theophylline), history of alcohol or other substance abuse, pregnant women, Alzheimer’s disease, mental retardation and other conditions (hearing and visual) that may hinder the patient’s ability to participate in the test for recall and memory; and the planned use of drugs that can possibly cause retrograde amnesia (scopolamine and atropine) were excluded. A written informed consent was obtained from all the patients.

Patients were assigned to the groupings used by Nishiyama, et al. Group A=20-39 years, Group B=40-59 years and Group C=60-79 years. Each age group was further divided into five groups according to the required dose of midazolam in mg/kg: Subgroup 1=0.01mg/kg, Subgroup 2=0.02mg/kg, Subgroup 3=0.03mg/kg, Subgroup 4=0.04mg/kg and Subgroup 5=0.05mg/kg. These values were based on common observation that a dose between 0.02 to 0.04mg/kg may render an average Filipino patient amnesic. Ten patients were assigned to each subgroup using the table of random numbers.

Data Collection

Demographic data of the patients were gathered. These included the age, sex, weight of the patients. Duration of the surgery or procedure was also recorded. All patients were placed on NPO for 8 hours. An intravenous fluid of D5NR 1L was started at maintenance rate. No sedative pre-medications were given to the patients. Upon transfer to the operating room, standard monitors were hooked (noninvasive BP, ECG, and pulse oximeter). Emergency resuscitation equipment was made available.

Adapting the principle used by Kain et al for testing memory, colored geometric cards were used in place of picture cards. These geometric cards are described as follows: 1) red square measuring 7-cm in length and width with no background, 2) green triangle measuring 8-cm on each of the two sides and 9-cm at the base with no background, and 3) yellow circle measuring 7.5-cm in diameter.
widest diameter.

There were two examiners involved in the study. While on the supine position, the first examiner asked the patient to identify the red square. This was shown approximately 1 foot away from the patient’s face. Then midazolam (Dormicum) was given intravenously based on the required dose determined. Oxygen was administered at 6 Lpm via a partial rebreathing mask. After 3 minutes, the first examiner asked the patient to identify the green triangle. Anesthesia for the patient was then given as planned. One or two hours after the procedure, when the patient was fully awake and responsive, recall and recognition for the colored geometric card(s) seen during baseline testing and post-medication testing was assessed. The patient was then asked by a second examiner to identify the geometric card(s) that the patient recalled seeing prior to administration of anesthesia. Persons blinded to the dose of the midazolam were the patient and the second examiner who tested for recall and recognition.

Data Processing And Analysis

Interpretation of Data Collected. Patients were classified according to their responses. An amnesia grade of 0 was given if patient recognized both the red square and green triangle post-operatively. An amnesia grade of 1 was given if the patient recognized only the red square post-operatively. The patient was excluded from the study if the red square was not recognized or the yellow circle was also recognized postoperatively or the patient was too sedated to complete the test.

Definition of Terms. Midazolam dose was labeled as required dose if the mg/kg dosage (i.e. 0.01, 0.02 mg/kg etc) was being referred to and as actual dose if the computed dose (e.g. 1 mg or 2 mg) was being referred to.

ED50 was used to indicate the minimum dose of midazolam wherein 50% of the study population of a particular age group was rendered amnesic.

Statistical Design. Demographic data were expressed as proportion, mean, and standard deviation. Probit analysis using SAS and Minitab 14 softwares determined the Effective Dose (ED)50 for each age group. Multiple logistic regressions was used in the analysis of the relationship of anesthesia dose and the resultant amnesia. Excel and SPSS ver.10 softwares were also used in the processing and analysis of the data. A P value of <0.05 was considered statistically significant.

RESULTS

There were 97 (64.3%) females and 53 (35.3%) males included in the study. Patients’ sex distribution did not differ for groups A and B where there were more females than males. On the other hand, group C had equal distribution of males and females. Three patients were excluded for recognizing the yellow geometric figure postoperatively. One patient was excluded for being too sedated to complete the test.

The mean weight of the study population and duration of anesthesia did not differ significantly across the different age groups (Table 1).

The ED50 value of midazolam which produced anterograde amnesia for all patients regardless of age group was 0.019 mg/kg. Putting age as a factor, the ED50 values for group A was 0.023 mg/kg, for group B was 0.020 mg/kg, and for group C was 0.017 mg/kg based on the required dose (Table 2 and Figure 1).

Across age groups, there was an increasing tendency towards amnesia as the required dose of midazolam

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sex distribution</th>
<th>Actual Dose (mg)</th>
<th>Age (Yr)</th>
<th>Body Weight (kg)</th>
<th>Duration (Hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>M: 14 (28%)</td>
<td>1.89 ± 1.0</td>
<td>30 ± 5.3</td>
<td>62.8 ± 13.3</td>
<td>2.2 ± 2.3</td>
</tr>
<tr>
<td>20-39 yr</td>
<td>F: 36 (72%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B</td>
<td>M: 14 (28%)</td>
<td>1.7 ± 0.8</td>
<td>48 ± 5.8</td>
<td>58.9 ± 12.9</td>
<td>2.1 ± 1.5</td>
</tr>
<tr>
<td>40-59 yr</td>
<td>F: 36 (72%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group C</td>
<td>M: 25 (50%)</td>
<td>1.7 ± 0.8</td>
<td>67 ± 5.9</td>
<td>60.1 ± 12.9</td>
<td>1.7 ± 1.9</td>
</tr>
<tr>
<td>60-79 yr</td>
<td>F: 25 (50%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All age groups</td>
<td>M: 53 (35%)</td>
<td>1.7 ± 0.9</td>
<td>49 ± 16</td>
<td>60.1 ± 12.6</td>
<td>1.9 ± 1.9</td>
</tr>
</tbody>
</table>

|                       | F: 97 (65%)      | |

TABLE 1. Demographic Data
TABLE 2. Effective doses of midazolam that caused amnesia in the different age groups

<table>
<thead>
<tr>
<th>AGE GROUPS</th>
<th>ED10 VALUE (mg/kg)</th>
<th>ED50 VALUE (mg/kg)</th>
<th>ED90 VALUE (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>0.01</td>
<td>0.023</td>
<td>0.053</td>
</tr>
<tr>
<td>Group B</td>
<td>0.01</td>
<td>0.020</td>
<td>0.036</td>
</tr>
<tr>
<td>Group C</td>
<td>0.01</td>
<td>0.017</td>
<td>0.027</td>
</tr>
<tr>
<td>All age groups</td>
<td>0.01</td>
<td>0.019</td>
<td>0.038</td>
</tr>
</tbody>
</table>

FIGURE 1. Probability Plot for Amnesia of different age groups based on required dose

increased. This tendency was greater for the older population of group C (Figure 2).

Based on the Chi-square test, there was a direct relationship in the category of the required dose for midazolam and the presence or absence of amnesia (p<0.001). Patients were more likely to have amnesia with increasing required dose (Table 3).

Based on the t-test, there was a significant difference in the mean actual dose of midazolam between those with amnesia and those without amnesia (p<0.001). The mean (2.1 ±0.8 mg) was significantly higher among those with amnesia compared to those without amnesia (1.13±0.8).

Using independent samples t-test, the mean age for those with amnesia was higher than for those who did not have amnesia. However, the difference was not found to be significant (p=0.07) nor was there sufficient evidence to say that the weights were different between those with amnesia and those without amnesia. There was also no sufficient evidence to say that the durations of the procedures/surgeries were different between those with amnesia and without amnesia.

Using simple regression, it was found that the required dose was a significant contributing factor in the resultant amnesia (p<0.001). The likelihood of having amnesia increased as the required dose increased (Figure 3).

Likewise, there was a significant relationship seen between actual dose and resultant amnesia (p<0.001). There was a fivefold chance of having amnesia for every unit
FIGURE 2. Number of patients with amnesia according to age group and required dose

TABLE 3. Distribution of patients according to amnesia score and required dose

<table>
<thead>
<tr>
<th>Required dose (mg/kg)</th>
<th>Amnesia Score = 1</th>
<th>Amnesia Score = 0</th>
<th>Total number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>1 (3.3%)</td>
<td>29 (96.7%)</td>
<td>30</td>
</tr>
<tr>
<td>0.02</td>
<td>19 (63.3%)</td>
<td>11 (36.7%)</td>
<td>30</td>
</tr>
<tr>
<td>0.03</td>
<td>25 (83.3%)</td>
<td>5 (16.7%)</td>
<td>30</td>
</tr>
<tr>
<td>0.04</td>
<td>27 (90%)</td>
<td>3 (10%)</td>
<td>30</td>
</tr>
<tr>
<td>0.05</td>
<td>27 (90%)</td>
<td>3 (10%)</td>
<td>30</td>
</tr>
</tbody>
</table>

FIGURE 3. Relationship between required dose and resultant amnesia
increase in the actual dose (Figure 4).

A multivariate analysis of the following factors: required dose, age, sex, weight and duration of procedure or surgery were done. Based on the final logistic regression equation, the significant contributing factors to amnesia were the required dose, age and sex.

Females were three times more likely to have amnesia than males, controlling for other factors such as age and required dose (Table 4). As the age increased, the chances of having amnesia also increased by 1.047 times. Controlling for the effect of the other factors, the chance of having amnesia also increased as the required dose increased. The duration of the surgery or procedure and weight were not found significant.

A second multivariate analysis was done using the actual dose as a variable instead of the required dose. Age, weight, duration, sex, and the actual dose of midazolam was subjected to logistic regression analysis. After the backward selection procedure, what remained as the significant contributing factors to resultant amnesia were actual dose, age, weight, and sex.

Females were also three times more likely to have amnesia than males, controlling for other factors such as age, weight and actual dose (Table 5).

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**TABLE 4.** Amnesia score of patients according to gender and required dose

<table>
<thead>
<tr>
<th>Required dose</th>
<th>Male</th>
<th>Female</th>
<th>Male(%)</th>
<th>Female(%)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01 mg/kg</td>
<td>11</td>
<td>18</td>
<td>1 (6.3)</td>
<td>0 (0)</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>0.02 mg/kg</td>
<td>6</td>
<td>5</td>
<td>3 (33)</td>
<td>16 (76)</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>0.03 mg/kg</td>
<td>4</td>
<td>1</td>
<td>12 (75)</td>
<td>13 (93)</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>0.04 mg/kg</td>
<td>1</td>
<td>2</td>
<td>9 (90)</td>
<td>18 (90)</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>0.05 mg/kg</td>
<td>1</td>
<td>2</td>
<td>5 (83)</td>
<td>22 (92)</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>28</td>
<td>30(56.6)</td>
<td>69 (71.7)</td>
<td>53</td>
<td>97</td>
</tr>
</tbody>
</table>
TABLE 5. Amnesia score of patients according to gender and actual dose

<table>
<thead>
<tr>
<th>Actual dose</th>
<th>Male</th>
<th>Female</th>
<th>Male(%)</th>
<th>Female(%)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 1 mg</td>
<td>12</td>
<td>21</td>
<td>2 (14)</td>
<td>9 (30)</td>
<td>14</td>
<td>30</td>
</tr>
<tr>
<td>1.1 – 2 mg</td>
<td>7</td>
<td>4</td>
<td>8 (53)</td>
<td>30 (88)</td>
<td>15</td>
<td>34</td>
</tr>
<tr>
<td>2.1 – 3 mg</td>
<td>2</td>
<td>2</td>
<td>15 (88)</td>
<td>24 (92)</td>
<td>17</td>
<td>26</td>
</tr>
<tr>
<td>3.1 – 4 mg</td>
<td>1</td>
<td>1</td>
<td>5 (71)</td>
<td>6 (86)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>23</td>
<td>28</td>
<td>30 (57)</td>
<td>69 (71)</td>
<td>53</td>
<td>97</td>
</tr>
</tbody>
</table>

As the age increased the chances of having amnesia also increased by 1.048 times. Weight appeared to be indirectly proportional to the likelihood of having amnesia, i.e. as the weight increased, the odds of having amnesia decreased compared to lower weights. Controlling for the effect of other factors, the patients more likely had amnesia as the actual dose increased. The duration of the surgery or procedure was not significantly related to the incidence of amnesia.

In the second multivariate analysis, the coefficient of multiple determination using Cox and Snell $R^2$ was slightly lower (0.388) than the first multivariate analysis (0.391). This may suggest that the first regression analysis model using the required dose as a variable may be a better predictor of amnesia than the model using actual dose as variable.

**DISCUSSION**

In this study, many factors that influence the levels of amnesia and sedation in patients given midazolam were identified. Lee, et. al. identified age and pre-procedural anxiety level which was influenced by gender, weight, and previous experience of conscious sedation to be related to amnesia and sedation. Differences in the pharmacokinetics of midazolam was also observed genetically and was found to be significantly different even between red-haired and brown-haired individuals. A study on British subjects reveals a 36% rate of amnesia caused by midazolam at a dose of 0.05 mg/kg. Miller studied American subjects, and reported that the dose of 0.07 mg/kg resulted in insufficient amnesia. Morin used an actual dose of 3 mg among German subjects and achieved amnesia in only 27% of 174 patients studied.

The results of this study revealed that Filipino subjects required lower doses of midazolam to induce amnesia. The ED50 value for midazolam based on the required dose was 0.019 mg/kg disregarding age as a factor. The mean actual dose that caused amnesia also revealed a lower dose of 2.1 ±0.8 mg.

Such racial differences in the response to a drug are explained by Burroughs, et al in an article and they cited several factors affecting it. These include environment, cultural, psychosocial, and genetic factors. Of the four, genetic factors are found to be the major determinants of the normal variability in drug effects. According to the article, these are affected by polymorphisms, which are naturally occurring variants in the structures of genes and the products they encode. The relevant gene products are drug metabolism enzymes, receptor proteins and other proteins involved in drug response or disease progression. Furthermore, the article stated that polymorphisms may influence a drug's action by altering its pharmacokinetic or pharmacodynamic properties. Clinically, there may be an increase or decrease in the intensity and duration of the expected drug effects and substantial dosage adjustments may be necessary for individuals from different population. Benzodiazepines are among those drugs found to be affected by such polymorphisms. A study on Asian psychiatric patients revealed lower dose requirements for diazepam. In another study, the clearance of alprazolam is significantly higher in whites than in Asian. This drug is metabolized by the CYP3A4 system. So far, there are no other studies of ethnic differences in response to midazolam and its resultant amnesia which support this present study.

Weight was not found to influence amnesia when the required dose was used. This was expected since weight was automatically factored in with the dose (mg/kg). However, when the actual dose was used to analyze the data on amnesia, weight had an indirect relationship with likelihood for amnesia, i.e. the heavier subjects had fewer tendencies for amnesia than the lighter subjects. The clinical relevance of this finding is appreciated in the following example: an actual dose of 1.5 mg may cause amnesia or even deep sedation to a 40-kg subject but may not affect a 90-kg subject at all. The coefficient of multiple
determinations may serve as basis to show that the required dose may be a better predictor of amnesia than the actual dose. This is consistent with a previous study done by Ishiguro wherein regression analysis revealed midazolam dose per body weight as one of the most important factors for the complete amnesia.

In this study, the age of the patient was another important factor found to influence the occurrence of amnesia. The older the patient the greater the chance of having amnesia at an effective dose of midazolam. In this study, the dose of 0.017mg/kg was effective in causing amnesia in 50% of the ederly age group. A dose of 0.03mg/kg resulted in 90% of subjects in the 60-79-year age group to have amnesia. This percentage was higher when compared to previous studies done on elderly subjects. After the administration of 0.03mg/kg of midazolam, Christe, et al noted 84% of 65 patients developing amnesia and Platten, et al noted 86% of 10 patients developing amnesia. Several studies revealed that amnesic and sedative effects of midazolam are proportionally related with age. Furthermore, these studies revealed a linear decrease of IV midazolam dosage for sedation with increasing age, i.e. a lower dose of midazolam is needed for sedation in older subjects. Greenblatt, et al proposed that this may be due to the increased sensitivity of the CNS to the effects of midazolam with increasing age. This is similar to the explanation presented by Jacobs, et al.

In previous studies, there were contradicting results regarding gender as a factor influencing occurrence of midazolam-induced amnesia or sedation. Some studies did not support gender as a significant factor in the development of sedation or amnesia among subjects given midazolam while other studies showed men are more sensitive to midazolam than women. These studies showed that a lower mean dose per kilogram for males is needed for sedation compared to females. The present study revealed that females were more susceptible to develop amnesia than males at an effective dose of midazolam. A possible explanation for this finding was that there were more females exposed to the required dose of 0.02mg/kg than males which resulted in a greater percentage of females having amnesia. However, using the data of actual dose and gender distribution, despite the fact that more males were exposed to a higher actual dose of >2.0mg, the multivariate analysis still showed the females to be more susceptible to amnesia than the males. Another possible explanation may be that the lower weights of females made them more susceptible to the amnesia induced by the given actual dose of midazolam. A study also correlated anxiety with higher midazolam dose requirement for sedation. Although not measured as a variable, males were perceived to be more anxious than the females in this present study. More males preferred to be given general anesthesia than sedation when given the option to choose.

CONCLUSION

In this study, it was shown that Filipino subjects required lower doses of midazolam to bring about amnesia. The ED50 values of midazolam that caused amnesia in Filipino subjects were as follows: group A (20-39 years) =0.023mg/kg, group B (40-59 years)=0.020mg/kg and group C (60-79 years)=0.017mg/kg. In clinical practice, it will be useful to know that the required dose may be a better predictor of amnesia than the actual dose, i.e. computing for the dose per weight may give better assurance that the patient will have amnesia. Increasing age decreased the requirement for midazolam. Older persons required a lesser dose to achieve amnesia. The duration of the procedure or surgery did not influence the incidence of amnesia. Because of the possibility of gender influencing midazolam-induced amnesia, it is recommended that future studies be made among Filipino subjects using gender as a controlled variable. Further studies should be done to determine whether females are really more susceptible to develop amnesia than males. Other variables that should be considered are the level of anxiety and the level of sedation of the patients.

REFERENCES

9. Williams TJ and Bowie PE. 1999 May. Midazolam sedation to produce complete amnesia for bronchoscopy: 2 years'
experience at a district general hospital. Respiratory Medicine, 93(5): 361-5.

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