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Midazolam Sedation for Percutaneous Liver Biopsy

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Control of patient respiration is needed to safely perform percutaneous liver biopsy (PLB) and may be adversely affected by sedation. The purpose of this study was to evaluate the safety of PLB with intravenous midazolam and to evaluate patient acceptance of PLB with and without sedation. Two hundred seventeen consecutive patients underwent 301 percutaneous liver biopsies. One hundred fifty-one of the biopsies were done after the patients were sedated with intravenous midazolam immediately before the biopsy. The last 61 patients were questioned after the biopsy to evaluate the discomfort of the procedure, their memory of the procedure, and their willingness to undergo another PLB. The major complication rate was similar in the midazolam-treated (0.7%) and untreated (0.7%) groups. The midazolam-treated patients had a numerically lower mean pain score (1.5 ± 0.4 vs 4.0 ± 0.7) ($\bar{x}$ ± SEM) (P = 0.07) and significantly lower mean memory score (4.8 ± 0.7 vs 9.9 ± 0.1) (P < 0.01) than the untreated patients. The treated and untreated groups had similar mean willingness for repeat PLB scores (9.3 ± 0.3 vs 9.1 ± 0.6). We conclude that: (1) there is no increased risk of PLB with midazolam and (2) patients have less memory of the procedure with midazolam.

KEY WORDS: midazolam; percutaneous liver biopsy.

Percutaneous liver biopsy (PLB) is associated with a significant degree of patient anxiety and discomfort (1). Current textbooks suggest using only local anesthesia and do not advise using intravenous sedation before percutaneous liver biopsy (2, 3). The performance of a liver biopsy requires the patient to assist the physician by stopping their respiratory movement during the biopsy. Sedation has not been used, as this may hinder patient compliance and possibly increase the complication rate.

Midazolam, a short-acting benzodiazepine, has been extensively used for intravenous sedation for gastrointestinal endoscopic procedures. In a recent publication, Brouillette et al reported performing liver biopsy with intravenous midazolam sedation. The patients treated with midazolam experienced less discomfort with the procedure, had less memory of the procedure, and showed a trend toward being more willing to undergo a repeat liver biopsy than those patients who were treated with placebo (1).

Since a liver biopsy done with midazolam appears to be a less unpleasant experience for patients than PLB without sedation, it would be extremely important to determine if this sedation is associated with an increased risk of procedure-related complications. Furthermore, the results of the Brouillette study are provocative, but due to the small number of patients studied, these results need confirmation.

The purpose of this study was to: (1) assess the risk of liver biopsy with midazolam premedication and (2) assess the patients' memory of the liver biopsy procedure, discomfort during the procedure,

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and willingness to undergo a subsequent percutaneous liver biopsy in patients given premedication with midazolam compared to a group of patients who underwent PLB by conventional methods.

MATERIALS AND METHODS

Subjects. All patients undergoing percutaneous liver biopsy by two experienced hepatologists at Northern Michigan Hospital between 1987 and 1992 were evaluated. Patients undergoing percutaneous liver biopsy prior to March 1, 1990, were evaluated retrospectively, while those patients undergoing biopsy after March 1, 1990, were evaluated prospectively. All patients studied had prothrombin times less than 3 sec greater than control, platelet counts greater than 80,000/μl, no clinically detectable ascites, and no history of xylocaine allergy. The study was approved by the Institution Research Review Board, and informed consent was obtained from all patients prior to liver biopsy.

Procedure. Two hundred seventeen patients underwent 301 percutaneous biopsies using a TruCut needle (Travenol Laboratories, Deerfield, Illinois). The same group of five gastrointestinal assistants assisted in all of cases. Biopsies were done after liver localization by physical examination in the endoscopy suite (87) or after ultrasound liver localization in the radiology suite (214). All patients received local anesthesia with 1% xylocaine before the biopsy was performed. Group A patients had biopsies performed by one hepatologist and received no intravenous sedation. Group B patients were biopsied by the second hepatologist and received intravenous midazolam immediately before the procedure. The midazolam was titrated in 0.5- to 1.0-mg increments until slurred speech was induced. Patients evaluated prospectively were questioned by one nurse 8 hr after the procedure. Patients were asked to answer the following questions pertaining to their liver biopsy: (1) On a scale of 0 to 10, how much discomfort did you experience with your liver biopsy yesterday? (2) On a scale of 0 to 10, what do you remember about the actual liver biopsy you had yesterday? (3) On a scale of 0 to 10, how willing would you be to undergo another liver biopsy in the future if one was medically necessary? (0 being "no" and 10 being "yes.")

All biopsies were used in the analysis of the complication rate of liver biopsy with and without midazolam. Only those patients studied prospectively were used in the analysis of the effect of midazolam on patient pain with, memory of, and willingness to undergo another liver biopsy.

Oxygen Saturation. All patients studied prospectively had continuous O_2 saturation measured by continuous pulse oximetry (Criticare Systems Inc., Waukesha, Wisconsin). The O_2 saturation immediately prior to the procedure and the lowest O_2 saturation during the periprocedure period were recorded.

Statistical Analysis. The Student's *t* test and chi-square analysis were used for statistical comparisons between groups.

TABLE 1. *

	Tx group (N = *38*)	*Control group* (N = *23*)	P *value*
Memory score	4.8 ± 0.7	9.9 ± 0.1	0.007
Pain score	1.5 ± 0.4	4.0 ± 0.7	0.07
Willingness for further PLB score	9.3 ± 0.3	9.1 ± 0.6	0.6

*Values are means ± SEM.

RESULTS

The patients in the treatment and nontreatment groups did not differ with respect to age, sex, and prebiopsy values of PTT, platelet count, bilirubin, AST, or alkaline phosphatase. The midazolam-treated patients had a higher prebiopsy mean prothrombin time (12.2 sec ± 0.1) ($\bar{x}$ ± SEM), than the untreated group (11.7 ± 0.1) ($P < 0.05$). The midazolam-treated patients also had a lower prebiopsy mean serum albumin level (3.8 ± 0.1 mg/dl) than the untreated group (4.0 ± 0.1; $P < 0.005$).

Ultrasound liver localization was used for 73% (110/151) of the biopsies in the midazolam-treated group and 69% (104/150) of the biopsies in the untreated group; 1.9% (3/154) of the needle insertions in the treatment group and 2.6% (4/154) of the insertions in the untreated group failed to recover liver tissue. Neither of these differences were significant.

The mean dose of midazolam used in the treatment group was 4.0 mg with a range of 1–17 mg. No patient in either group had a decrease in oxygen saturation of greater than 10% from baseline values.

There was one minor complication 0.7% (1/151) and one major complication 0.7% (1/151) in the treatment group. Similarly, there was one minor 0.7% (1/150) and one major 0.7% (1/150) complication in the untreated group. Both minor complications were vasovagal reactions. Both major complications were bleeds that were managed nonoperatively but did require blood transfusions. There were no deaths related to the liver biopsy procedure in either group. Table 1 lists the mean memory, pain, and willingness to undergo repeat liver biopsy scores for both groups. The treated patients had less memory of the procedure. The pain score was numerically lower in the treatment group, but this difference was not statistically significant. There was no difference in the willingness for repeat PLB scores between the treatment and nontreatment groups.

DISCUSSION

We found no increase in major or minor complications of PLB with the use of midazolam. Likewise, we found no clinically significant oxygen desaturation with the use of midazolam-induced sedation.

Our data suggest that midazolam use before PLB is not associated with an increase in procedure-related complications. Despite the higher mean PT level and lower mean albumin level in the treatment group, suggesting more severe hepatic dysfunction in this group, there was no difference in the bleeding rate between the two groups.

One potential source of error in the study could be related to different physician techniques. Although this is certainly possible, we do not feel this was of much significance, as both physicians were experienced hepatologists with a similar complication record with PLB prior to the commencement of this study. Moreover, both physicians used the same equipment, did a similar number of cases under ultrasound localization, and had a similar percentage of empty passes. Both physicians also used the same nursing staff during the periprocedural period and had the same nurse complete the postprocedure questionnaire with the patients.

The bleeding rate per biopsy (0.7%) and per patient (0.9%) in both groups is within the range (0.32%–2.8%) reported in recent series (4–6).

These results were very similar to those of Brouillette et al. Brouillette's patients had statistically significantly less pain ($P < 0.04$) and less memory ($P < 0.001$) (1). Although our difference for pain score was not statistically significant, the P value (0.07) was fairly close to that of Brouillette et al (1).

In summary, we found no increased risk of PLB with midazolam sedation. Patients treated with midazolam had less memory of the biopsy procedure and numerically, but not statistically, significantly less discomfort with the procedure than untreated patients. Midazolam sedation appears to be safe and to make PLB a more pleasurable experience. However, we caution the readers that this is a preliminary investigation; clearly, a greater number of patients needs to be studied before the safety of midazolam sedation for PLB can be firmly established.

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REFERENCES

1. Brouillette D, Yoo Y, Chien M, Rabinovitz M, Tarter R, Van Thiel D: Use of midazolam for percutaneous liver biopsy. Dig Dis Sci 34:1553–1558, 1989
2. Drossman D: Manual of Gastrointestinal Procedures. New York, Raven Press, 1987
3. Schiff L, Schiff ER: Diseases of the Liver. Philadelphia, JB Lippincott, 1987
4. McGill DB, Rakela J, Zinsmeister AR, Ott BJ: A 21-year experience with major hemorrhage after percutaneous liver biopsy. Gastroenterology 99:1396–1400, 1990
5. Piccinino F, Sagnelli E, Pasquale G, Giusti G: Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. J Hepatol 2:165–173, 1986
6. Knaver CM: Percutaneous biopsy of the liver as a procedure for outpatients. Gastroenterology 74:101–102, 1978