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Self-reported recovery time of daily activity after bone marrow harvesting from healthy donors

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Abstract

Purpose. The study was planned to describe and compare the resumption of daily activity after bone marrow harvesting (BMH) under general anesthesia with different anesthetic agents, isoflurane, sevoflurane and propofol.

Methods. Sixty-five adult healthy allogenic donors (26 women, 39 men; 37.0 ± 9.5 years of age; ASA class I or II) were studied. BMH was performed under general anesthesia with isoflurane, sevoflurane, or propofol as the main anesthetic agent. On day 1, donors were asked how soon they could resume five daily activities: talking, walking, drinking, eating, and reading.

Results. Although there was considerable variation in resumption time within and among these five activities, 77% of donors resumed all of these basic daily activities within 12 h after BMH. Donors who received propofol resumed talking significantly faster than those who received sevoflurane or isoflurane, but the choice of main anesthetic agent did not affect the time of resumption of other activities. Lower preoperative hemoglobin concentration and greater decline of hemoglobin concentration on day 1 were significantly associated with slower resumption of walking and reading.

Conclusion. Although the choice of main anesthetic agent and anemia affected postoperative recovery, 77% of donors could resume these five daily activities within 12 h.

Key words Bone marrow donors · Bone marrow harvesting · General anesthesia · Self-reported recovery time of daily activity

Introduction

Allogenic bone marrow transplantation is now the established therapy for hematological disorders [1]. In addition to numerous marrow donations from related donors, more than 2000 unrelated donors in Japan have undergone general anesthesia for bone marrow harvesting (BMH) since the foundation of the Japan Marrow Donor Program (JMDP). Because donors are healthy volunteers and BMH is a simple procedure, how soon they can anticipate a return to normal life should be their major concern. However, there is little documented information for bone marrow donors about a clear timetable of postoperative recovery landmarks such as eating, drinking, and mobility. The effects of anesthetic choice on the rate and profile of resumption of daily activities have not been clarified either.

The purpose of this study was to characterize donors' recovery from general anesthesia for BMH as their self-reported recovery time of daily activity, and to compare it among donors who received different main anesthetic agents: isoflurane, sevoflurane and propofol. Specifically, this prospective study was designed to evaluate three questions: "How long does it take for donors to resume their basic daily activities?" "Does the choice of main anesthetic agent affect the resumption time?" "What factors are associated with slow resumption?"

Materials and methods

The study was approved by the institutional review board of the Institute of Medical Science, University of Tokyo. The subjects were 65 healthy (ASA class I or II) adult allogenic bone marrow donors who underwent BMH procedures in the surgical center of the Institute of Medical Science, University of Tokyo, during the period from July 1996 to September 1998. Informed consent was obtained from all of the donors at their pre-anesthetic visit.

On the day of BMH, donors were premedicated with hydroxyzine 25 mg and atropine sulfate 0.5 mg i.m. 30 min before arriving at the operating room, where they were monitored by ECG, noninvasive measurement of

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blood pressure, pulse oximetry, capnography, and rectal temperature.

Donors received either isoflurane, sevoflurane, or propofol as the main anesthetic agent. We randomly allocated the first 40 cases into sevoflurane or isoflurane anesthesia groups, but after propofol had become available, we anesthetized all donors with propofol (25 cases). In the case of donors who received isoflurane or sevoflurane, anesthesia was induced with thiopental 5 $mg \cdot kg^{-1}$, followed by vecuronium bromide 0.1 $mg \cdot kg^{-1}$. They received isoflurane 3% or sevoflurane 3% before tracheal intubation. After the donors were placed in the prone position, pentazocine 5 to 15 mg was administered, and anesthesia was maintained with either isoflurane or sevoflurane 0.5%–1.5% with 66% nitrous oxide in oxygen. In the case of donors who received propofol, anesthesia was induced with propofol 2 $mg \cdot kg^{-1}$ and fentanyl 0.1 mg, followed by vecuronium bromide 0.1 $mg \cdot kg^{-1}$ and maintained with propofol 3–5 $mg \cdot kg^{-1} \cdot h^{-1}$ with 66% nitrous oxide in oxygen. Two experienced anesthesiologists anesthetized all of the donors. They maintained anesthesia to control blood pressure within ± 20% of the pre-anesthetic value and end-tidal CO_2 between 30 and 40 mmHg. They also tried to provide rapid emergence from anesthesia.

Bone marrow was harvested from the posterior iliac crest with a 13-G needle. The marrow harvest volume was decided according to the recipient's body weight. Sixty-two donors predonated autologous blood 3 weeks before BMH. The volume of predonated autologous blood was decided according to the planned harvest volume. Donors received all of their predonated autologous blood during the surgery.

At the end of BMH, the residual effect of the muscle relaxant was reversed by neostigmine 0.05 $mg \cdot kg^{-1}$ with atropine sulfate 0.02 $mg \cdot kg^{-1}$. After the donors were extubated and fulfilled our five immediate recovery criteria (spontaneous eye opening, ability to breath deeply and cough out phlegm, $SpO_2 > 97\%$ after breathing room air for 5 min, ability to move all extremities, and blood pressure within 20% of pre-anesthetic value), they were transferred directly to the ward.

Within 2 h after discharge, the donors were offered something to drink for the first time, and if no problem was observed, they were offered a light meal soon after that. At about the same time, they were also asked to try to stand up and walk around in the ward.

On day 1, donors were asked to complete a questionnaire (Appendix 1). The questionnaire was developed to evaluate their self-reported recovery time of five daily activities: talking, walking, drinking, eating, and reading.

The following information was obtained from medical records: (1) Anesthesia time (the interval between induction and discontinuation of anesthesia); (2) "harvest time" (the interval between the start and the completion of marrow harvesting); (3) immediate recovery time (the interval between discontinuation of anesthetics and attainment of the immediate recovery criteria); (4) pre-Hb (hemoglobin concentration within one week before BMH); (5) Hb-drop (difference between pre-Hb and hemoglobin concentration on day 1); (6) postoperative nausea and vomiting (PONV); and (7) prescription of analgesics after BMH.

Statistical analysis

To investigate the determinants of self-reported recovery time, donors were dichotomized into fast-recovery and slow-recovery group according to the median values for each of the five activities, and medical variables were compared between these two groups by Student's *t*-test, the chi-square test, and the Wilcoxon rank-sum test. To adjust for the effects of likely confounding factors in analysis of these associations, a logistic regression model was also used. Data were analyzed with STATA version 6.0 (Stata, College Station, TX, USA). A P value < 0.05 was considered to be statistically significant.

Results

All procedures were performed in the morning. Demographic and bone marrow harvesting characteristics are shown in Table 1. All of the donors met the immediate recovery criteria and were discharged from the operating room within 25 min after discontinuation of anesthesia. No donor had severe complications during anesthesia. No donor had prolonged hemorrhage or infection at the harvesting site. Six of the donors complained of postoperative nausea and vomiting (PONV); five asked for analgesics for pain at the donation site. There was no significant difference in demographic and bone marrow harvesting characteristics among donors who received different main anesthetic agents (data not shown).

Figure 1 shows the self-reported recovery times of daily activities in each category. There was a marked difference in recovery pattern. Within 2 h after surgery, more than 70% (47/65) of the donors were able to talk, but less than 20% had resumed eating and reading. However, within 12 h, 77% (50/65) of donors resumed all of these five activities. The median value was within 1 h for talking, within 2 h for drinking, and within 6 h for walking, eating, and reading.

There was no significant difference in age and sex between fast and slow recovery groups in each activity (data not shown). For walking, the Hb-drop was

significantly larger in the slow-recovery group (2.1 ± 1.1 mg·dl^{-1}) than in the fast-recovery group (1.2 ± 1.1 mg·dl^{-1}) (Student's *t*-test, $P < 0.01$). For eating, both the anesthesia time and the harvest time were significantly longer in the slow-recovery group (101 ± 23 and 71 ± 22 min, respectively) than in the fast-recovery group (91 ± 17 and 61 ± 15 min, respectively) (Student's *t*-test, $P = 0.04$). For reading, pre-Hb was significantly lower in the slow-recovery group (13.5 ± 1.5 mg·dl^{-1}) than in the fast-recovery group (14.4 ± 1.5 mg·dl^{-1}) (Student's *t*-test, $P = 0.02$).

Table 2 shows the recovery of talking according to main anesthetic agent. The proportion of the fast-recovery group members was significantly different among these three groups (chi-square test, $P = 0.03$) and was the highest among donors who received propofol. In other activities, there was no significant difference in recovery pattern among donors who received different main anesthetic agents (data not shown).

Table 3 shows the results of logistic regression analysis. After adjustment for likely confounding factors, there were significant associations between the choice of main anesthetic agent and recovery of talking. Pre-Hb and Hb-drop were found to be significantly

Table 1. Donors' characteristics and bone marrow harvest characteristics

Variable	Value[a]
Total no. of donors	65
Age (yr)	37.0 ± 9.5
Sex	
Male	39
Female	26
ASA class	
I	51
II	14
Main anesthetic agent	
Isoflurane	18
Sevoflurane	22
Propofol	25
Weight (kg)	61.7 ± 9.7
Height (cm)	165.5 ± 8.3
Harvest volume (ml)	934 ± 238
Harvest volume per unit weight (ml·kg^{-1})	15.4 ± 4.1
Harvest time (min)	66 ± 19
Anesthesia time (min)	95 ± 21
Immediate recovery time (min)	19 ± 3
Predonated autologous blood (ml)	545 ± 188
Preoperative Hb (mg·dl^{-1})	13.9 ± 1.5
Postoperative Hb (mg·dl^{-1})	12.4 ± 1.7
Hb drop (mg·dl^{-1})	1.5 ± 1.2

[a] Plus–minus values are means ± SD

Table 2. Number of donors in fast- and slow-recovery groups in the activity "talking" with different main anesthetic agents[a]

Main anesthetic agent	Fast-recovery group	Slow-recovery group
Isoflurane	6	12
Sevoflurane	10	12
Propofol	18	7

[a] Chi-square test, $P = 0.03$

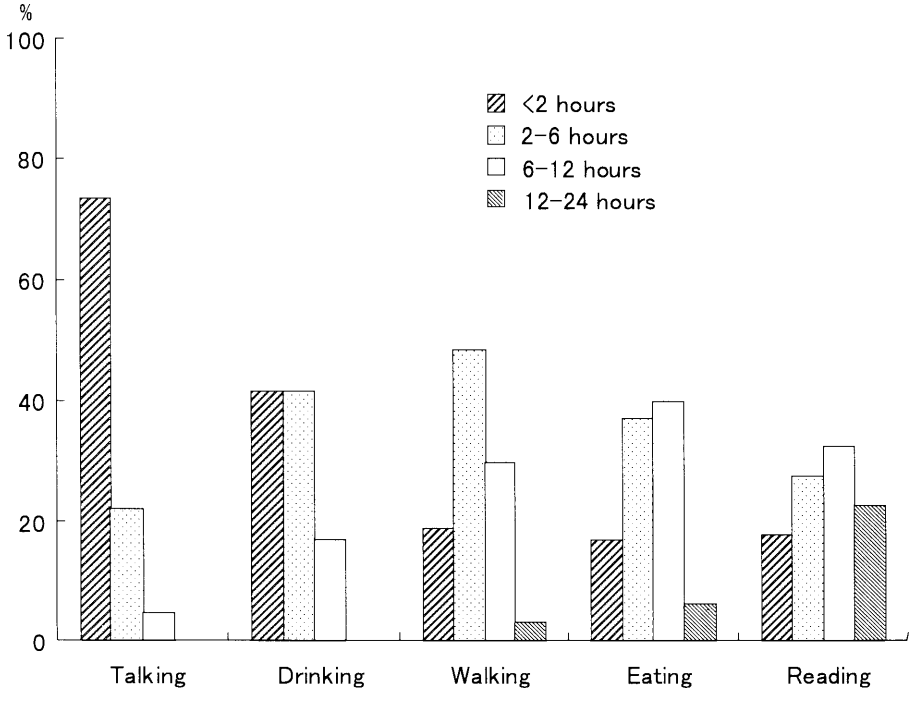

Fig. 1. Self-reported recovery time of daily activity after bone marrow harvesting. The response choices related to talking differed from the response choices related to other items. We used the same scale here to show the difference between activities. The detailed data on talking within a 2-h period are <0.5 h, 20.3%; 0.5–1 h, 32.8%; 1–2 h, 20.3%

Table 3. Odds ratios (95% confidence intervals) for factors associated with being in the slow-recovery group for each item (logistic regression model)[a]

Factor	Talking	Drinking	Walking	Eating	Reading
Age	—	—	—	1.07 (0.99–1.14)	1.05 (0.98–1.12)
Female sex	2.70 (0.68–7.62)	0.28 (0.06–1.34)	0.47 (0.06–3.71)	—	0.84 (0.10–6.97)
Harvest volume	—	1.00 (0.99–1.00)	—	—	—
Harvest time	—	1.01 (0.97–1.05)	1.02 (0.98–1.06)	1.02 (0.98–1.05)	1.00 (0.97–1.05)
Preoperative Hb	—	—	0.42 (0.17–1.07)	—	0.44* (0.21–0.95)
Hb drop	1.54 (0.92–2.57)	1.35 (0.78–2.36)	3.63* (1.39–9.44)	1.48 (0.90–2.44)	2.71* (1.25–5.90)
Sevoflurane/ propofol	5.30* (1.25–22.44)	0.94 (0.19–4.67)	0.43 (0.08–2.38)	0.32 (0.07–1.46)	0.37 (0.08–1.64)
Isoflurane/ propofol	4.88* (1.16–20.48)	0.71 (0.11–4.65)	0.80 (0.15–4.22)	1.25 (0.32–4.81)	0.66 (0.15–3.02)

* $P < 0.05$

[a] For each activity, variables whose univariate test had a P value < 0.25 were entered into the model

We did not include anesthesia time into the model because it was highly correlated with harvest time ($r = 0.9$, $P < 0.01$)

Since anesthetic agent was a categorical variable, we omitted propofol as the baseline category; the odds ratios were calculated for isoflurane and sevoflurane, with propofol as the baseline

associated with resumption of walking and reading. For eating, there was no significant association between harvest time and recovery after adjustment for other factors.

Discussion

It is important for anesthesiologists to provide patients not only with safe anesthesia but also with safe and expeditious recovery if the quality of care is to be raised. Recovery from general anesthesia encompasses early, intermediate, and late stages [2]. The late stage of recovery, when complete recovery of cognitive and psychological functions is being achieved, is characterized by the patient's resumption of activities of daily living.

The results of this study provide a timetable of post-anesthetic recovery landmarks, such as eating, drinking, and mobility, which are the highest-priority information that patients want to be given by the anesthesiologist [3]. In spite of significant variation within and among these five activity categories, 77% of donors reported that they resumed these activities within 12 h. Of these five activities, the resumption of talking was much faster than other activities, and the slowest was the resumption of reading. Interpretation of the resumption of reading was, however, somewhat difficult, because this item differs in nature from others. Talking, walking, drinking, and eating are basic and essential daily activities. Medical staffs repeatedly speak to patients immediately after the surgery and encourage them to drink, eat, and walk as soon as possible. Patients read, however, because they want to, not because of necessity. Interpretation of this item would have been easier if we had evaluated motivation and activity separately.

Of the various medical factors, perioperative hemoglobin concentration and choice of main anesthetic agent affected the recovery. Since a large amount of bone marrow is aspirated in a short period of time, it is not surprising that hemoglobin concentration had considerable effect on the speed of recovery.

Resumption of talking was significantly faster after propofol anesthesia than after isoflurane or sevoflurane, but there were no significant differences in other activities. What should be noted here is that the resumption of talking was much faster than that of other activities. This means that significantly faster recovery from propofol anesthesia was observed immediately after the surgery, but after a few hours, the recovery status was not different among these three anesthetic agents. Milligan et al. [4] reported similar results. They compared propofol and isoflurane anesthesia and also reported that initial recovery was more rapid in the propofol group, but that 1 h after surgery, there was no difference. Propofol is often chosen in a simple procedure such as ambulatory surgery because of its rapid emergence [5–7]. However, our findings, along with the findings of Milligan et al. [4], suggest that we cannot judge propofol to be superior solely from the patient's

condition immediately after surgery: recovery after discharge from the operating room must also be considered.

Although PONV and postoperative pain are associated with slow recovery and late discharge in outpatients [8], the incidence of PONV and prescription of analgesia were very low, and they were not found to be major problems after BMH.

There are several limitations in the methodology. First, we used pentazocine as an additional analgesic for sevoflurane and isoflurane anesthesia, whereas we used fentanyl for propofol anesthesia. Since pentazocine has a longer duration of action than fentanyl [9], it might have affected the result. However, this is unlikely, because the dose of pentazocine used (5–15 mg) was small. Second, because propofol was not available from the beginning of the study, we could not randomly allocate donors into three groups with respect to the main anesthetic agents. However, it is unlikely that this could seriously affect the result, because the donors are a homogeneous population who have undergone strict health checkups and we further adjusted for potential cofounders using multivariate analysis. Third, the time scales in response choices are broader as the time goes by, and this might have lowered the sensitivity in detection of clinically important differences in recovery after 6 h.

To conclude, we described self-reported recovery time of daily activity after BMH. Although anemia and the choice of main anesthetic agent were significantly associated with the speed of recovery, 77% of donors resumed all reported daily activities within 12 h. This information will be helpful in assuring potential donors of their explicit recovery landmarks after BMH and obtaining informed consent from them.

Appendix 1. The questionnaire about the resumption of daily activities after BMH

How soon have you become able to perform these activities after coming back from the operation room?

(Please circle one of the response choices most suitable to describe your state of recovery after BMH.)

1. "talking" (conversing with your doctor, nurses, family, etc.)
2. "walking" (standing up and moving on foot around the ward)
3. "reading" (reading any books, magazines, and newspapers you wanted to)
4. "drinking" (after drink is offered by your doctor or nurses)
5. "eating" (after food is offered by your doctor or nurses)

Response choices
Item 1 (talking)

1. <0.5 h
2. 0.5–1 h
3. 1–2 h
4. 2–6 h
5. 6–12 h
6. 12–24 h

Items 2–5*

1. <2 h
2. 2–6 h
3. 6–12 h
4. 12–24 h

*There is no response choice for less than 1 h for activities other than "talking," because it is not applicable.

References

1. Thomas ED, Blume KG, Forman SJ (1998) Hematopoietic cell transplantation, 2nd edn. Blackwell Science, Oxford
2. Smith I, White PF, Nathanson M, Gouldson R (1994) Propofol. An update on its clinical use. Anesthesiology 81:1005–1043
3. Lonsdale M, Hutchinson GL (1991) Patients' desire for information about anaesthesia. Anaesthesia 46:410–412
4. Milligan KR, O'Toole DP, Howe JP, Cooper JC, Dundee JW (1987) Recovery from outpatient anesthesia: a comparison of incremental propofol and propofol-isoflurane. Br J Anaesth 59:1111–1114
5. Kortilla K, Ostman P, Faure E, Apfelbaum Jl, Prunskis M, Ekdawi M, Roizen MF (1990) Randomized comparison of recovery after propofol-nitrous oxide versus thiopentone-isoflurane-nitrous oxide anaesthesia in patients undergoing ambulatory surgery. Acta Anaesthesiol Scand 34:400–403
6. Doze V, Shafer A, White P (1988) Propofol-nitrous oxide versus thiopental-isoflurane-nitrous oxide for general anesthesia. Anesthesiology 69:63–71
7. Valanne J (1992) Recovery and discharge of patients after long propofol infusion *vs* isoflurane anaesthesia for ambulatory surgery. Acta Anaesthesiol Scand 36:530–533
8. Twersky R (1998) Recovery and discharge of the ambulatory anesthesia patient. In: 49th Annual Refresher Course Lectures and Clinical Update Program. American Society of Anesthesiologists
9. Jeffe JH, Martin WR (1990) Opioid analgesics and antagonists. In: Gilman AG, Rall TW, Nies AS (eds) Goodman and Gilman's the Pharmacological basis of therapeutics, 8th edn. Pergamon, New York, pp 485–521