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Why do Women Use Midazolam in the Third Stage of Labor? An Exploratory Study

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Abstract

Aims: The aims of this study were to report women's reasons for using midazolam in the third stage of labor after the delivery of the fetal head, and report their knowledge of, attitudes toward, and satisfaction with its use.

Methods and Materials: This prospective study was conducted between November 1, 2019 and November 1, 2020. Inclusion criteria were age 18 years or older, admitted for labor or induction of labor, and with prior knowledge of midazolam. The women's reasons, knowledge, attitudes, perceptions, and satisfaction were recorded and analyzed.

Results: We recruited 200 women, mean age 29.4 years, 61% of whom knew about midazolam. Their reasons for choosing to have midazolam were relief of pain associated with the delivery of the fetal head, fear of delivery of the fetal head, and a desire to forget delivery details in 74%, 15%, and 11%, respectively. The factors that correlated positively with the women's reasons for choosing midazolam included younger age, higher parity, and source of information due to being used in previous deliveries (all *p*-values were <0.05). Satisfaction was high in 88.5% of women. The factors that correlated positively with higher satisfaction included the women's positive feeling about not recalling delivery details, and positive attitude toward the use of midazolam (all *p*-values were <0.05).

Conclusion: The women chose to have midazolam for relief of pain associated with the delivery of the fetal head, fear of delivery of the fetal head, or a desire to forget delivery details. This reflects deficiencies in antenatal pain management counseling and the presence of barriers against the use of epidural analgesia.

Keywords: Labor analgesics, labor pain, midazolam, satisfaction, third stage of labor

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INTRODUCTION

Labor and delivery are dynamic processes and women's experiences vary widely. Furthermore, childbirth is often very painful and labor pain scores very high on pain scales, being among the most painful life experiences. [1]. Fortunately, the memory of painful labor is short-lived and often forgotten within a few months after delivery [2]. Some women fear not only the pain, but also the labor and delivery and may request a caesarean section (CS) to avoid it all [3]. Women's perception of labor pain varies; while some cope well without interventions, others may request analgesics. [4]. In addition, postpartum depression is a prevalent condition. Beck et al. [5] showed that it affects approximately 10–15% of adult

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mothers every year and may persist for more than six months in 25–50% of affected mothers. Additionally, effective pain management during labor in the form of epidural analgesia has been shown to reduce the risks of postpartum depression [6].

There are various methods of labor pain management, such as relaxation therapy, acupuncture, massage, inhalational gases, parenteral medications, and regional analgesia [7]. A Cochrane review of the use of opioids during labor showed that their use provides some pain relief but is often associated with side effects such as drowsiness, nausea and vomiting [8]. Midazolam, however, is a short-acting benzodiazepine that has sedative, hypnotic, anxiolytic, and amnesic properties. In addition, it has a rapid onset of action after intravenous (IV) administration and short duration of action [9]. Midazolam is used for non-obstetric procedural sedation during pregnancy [10], as well as during labor and delivery, when preoperative midazolam has been shown to reduce anxiety associated with surgical termination of pregnancy [11]. Additionally, Salimi et al. [12] showed that intrathecal midazolam significantly enhanced the analgesic effect of opioids. Furthermore, premedication with midazolam during CS has been associated with a significant reduction in maternal anxiety scores without neonatal adverse effects [13]. It is also used in the third stage of labor during the manual removal of a retained placentae [14]. During the same stage, midazolam has been used immediately after the delivery of the fetal head and umbilical cord clamping because of its sedative, hypnotic, and amnesic properties. It is unclear where and how this practice started, and the authors of this paper are not advocates of this use of midazolam. Additionally, to the best of our knowledge, there are no published reports about this particular use.

The primary aim of this study was to explore the use of midazolam from the perspective of women in labor, including their reasons for choosing it and their knowledge of, and attitudes to, its use. We also explored women's satisfaction and complications in regard to the drug.

METHODS AND MATERIALS

This prospective exploratory study took place in the Department of Obstetrics and Gynaecology of a major general hospital between November 1, 2019 and November 1, 2020. Inclusion criteria required the women to be 18 years of age or more, 37 weeks or more pregnant, have a singleton alive pregnancy, be admitted to the hospital in labor or for induction of labor (IOL), and have knowledge about the use of midazolam in the third stage of labor after the delivery of the fetal head and umbilical cord clamping. To minimize bias, every other woman who was admitted to the labor ward and had knowledge of this use of midazolam was approached to participate. For the purpose of this study, 'knowledge' was defined as women's awareness of this use of midazolam and its effects. Women were followed up during labor and delivery and in the postpartum period. Women were excluded if they had known psychiatric illnesses, had epidural analgesia during the course of labor, had an emergency caesarean section, or decided not to continue with the research.

On admission, data were gathered on the women's characteristics, including age, body mass index (BMI), educational achievement, numbers of previous deliveries, gestational age, and if labor was spontaneous or the woman was admitted for IOL (and what was the indication for IOL). In addition, women's knowledge about midazolam was measured on a Likert scale (LS) using the choices of: not knowledgeable about but had heard about it; somewhat knowledgeable about it; knowledgeable about it; and, very knowledgeable about it. The source of women's information about midazolam was also recorded. Furthermore, women's reasons for choosing to have midazolam were reported. These reasons were identified from a prior pilot study which included 30 women who had used midazolam in previous deliveries. Their reasons were pain relief, fear of the delivery of the fetal head, or the desire to forget delivery details. The women's attitudes towards the use of midazolam were also measured on a LS using the choices of strongly disagree, disagree, no

opinion or uncertain, agree, and strongly agree. In addition, they were asked about the reasons why they did not choose epidural analgesia.

Regarding midazolam, the data collected included dosage, onset, duration of action, effects, and serious side effects, such as respiratory depression, cardiac arrest, and agitation. Additionally, the duration and method of monitoring after administration were recorded.

Immediately after delivery, data were collected on skin to skin contact (SSC) and if breastfeeding had been initiated within the first hour of delivery or not. The morning after delivery, data were collected on how much women recalled of the delivery details using both a visual analogue scale (VAS) and LS using the options of very high, high, moderate, low, or very low, as well as women's satisfaction with the use of midazolam using both a VAS and LS using very low, low, moderate, high, or very high choices. In addition, the women were also asked to rate their feeling about being unable to recall the delivery details using a LS of very good, good, average, bad or very bad.

Statistical Analysis

A convenience sampling method was applied to this study. Data analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY. Continuous variables were expressed by means and standard deviations, and categorical variables were shown as frequencies and percentages. Variables were regrouped for better comparison. To study the variables that influenced women's reasons for choosing to have midazolam, a multinominal logistic regression was used with the woman's reason as the outcome variable. The model used in the analysis was a good fit for the data (Chi-square = 102.4, df = 58, *p*-value <0.001).

The women's satisfaction with the use of midazolam was measured using both a VAS and LK. For VAS, an ordinal logistic regression was used, and the model fit the data well (Chi-square = 90.03, df = 22, *p*-value <0.001). The R software from R Core Team was used for this analysis (2020; R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

To study satisfaction as measured on a LS, a multinominal logistic regression was used, and the model fit the data well (Chi-square = 90.03, df = 22, *p*-value <0.001). Ethical approval was locally granted by the Institutional Review Board of the Specialty Hospital.

RESULTS

Two hundred women were recruited with a mean age (SD) of 29.4 (5.1) years and mean BMI (SD) of 28.6 (5.3) kg/m^2. In addition, 178 women (89%) were non-smokers, and 190 women (95%) had no known drug allergies. Furthermore, 23 women (11.5%) were primigravidae and 177 (88.5%) were multiparous. The results showed that 98.5% of the women had regular antenatal care. None of the women had an epidural analgesia as it was an exclusion criterion.

Midazolam: Women's Knowledge and Attitudes

Table 1 summarizes women's knowledge about midazolam and its sources, their reasons for requesting midazolam, and their attitudes towards its use, along with their feelings if they were refused midazolam. None of the women in this cohort had skin to skin contact (SSC) or initiated breast feeding within one hour of delivery. Table 2 shows the details of the gestational age, types of labor (spontaneous or IOL), indications for IOL, and reasons why women did not choose an epidural.

Table 1: Women's knowledge, information sources, reasons for using midazolam, attitude toward its use, and feeling if declined midazolam

Variable	Category	No.	Percentage
Knowledge about midazolam use with the delivery of the fetal head	Very knowledgeable	8	4.0
	Knowledgeable	29	14.5
	Somewhat	145	72.5
	Not, but heard about it	18	9
Source of knowledge about this particular use of midazolam	Previous use	151	75.5
	Friend/relative	25	12.5
	Social media	9	4.5
	Healthcare workers	15	7.5
Reasons why women would like to have midazolam	Pain relief	148	74
	Fear of delivery of fetal head	30	15
	Desire to forget delivery details	22	11
Attitude towards having midazolam in labor	Strongly agree	89	44.5
	Agree	98	49
	No opinion	9	4.5
	Disagree	4	2
Woman's feeling if refused midazolam	Very bad	63	31.5
	Bad	74	37
	Average	45	22.5
	Good	14	7
	Very good	4	2

Table 2: Pregnancy and Delivery Details

Variable	Number	Percentage
Labor		
• Spontaneous	149	74.5
• Induction of labor	51	25.5
Indications for induction of labor in 51 women (25.5%)		
• Post-term pregnancy	26/51	51
• Maternal request	31/51	25.5
• Pregnancy complications	10/51	19.9
• Pre-labor rupture of the fetal membranes	2/51	3.9
Reasons why women did not choose an epidural in this labor		
• Fear of epidural procedure and its complications	111	55.5
• Financial reasons	73	36.5
• Previous bad experience with an epidural	16	8

Midazolam Data

The mean (SD) for midazolam dose was 5.5 (0.3) mg. Table 3 shows the onset and duration of action, effects, side effects, and paradoxical effects in addition to the duration of monitoring. Our results showed that 16 women (8%) developed hyperactivity/agitation.

Table 3: Midazolam, dose, onset, duration of action, and duration of monitoring

Variable	Number	Percentage
Onset of action		
• 1–3 minutes	189	94.5
• 3–5 minutes	8	4.0
• No response	3	1.5
Duration of action		
• 1–9 minutes	4	2.0
• 10–19 minutes	27	13.5
• 20–29 minutes	57	28.5
• 30–59 minutes	104	52.0
• 60–120 minutes	5	2.5
• No response	3	1.5
Effects		
• Sedation	96	48.0
• Hypnosis	85	42.5
• No response	3	1.5
Side / Paradoxical effects		
• Agitation	16	8
• Bradycardia	1	0.5
Duration of monitoring		
• 0–29 minutes	14	7.0
• 30–59 minutes	53	26.5
• 60–89 minutes	131	65.5
• 90–120 minutes	2	1.0

Midazolam: Women's Perceptions

Regarding the recall of delivery details, 42% of the women reported low or very low levels. Furthermore, 66% said that they felt either good or very good about not being able to recall the delivery details. In addition, 95.5% said that they would use midazolam for future deliveries. On a LS, the overall satisfaction with the use of midazolam was high or very high in 88.5%, and on a VAS, the mean (SD) for satisfaction was 8.2 (2.0), as seen in Table 4.

Table 4: Women's perception of the use of midazolam (VAS: visual analogue scale. SD: standard deviation)

Variable	Mean (SD)		
Recall of delivery details: VAS	(3.2) 4.7		
Satisfaction: VAS	(2.3) 8.2		
Variable	**Category**	**No.**	**Percentage**
Recall of delivery details	Very high	25	12.5
	High	55	27.5
	Moderate	36	18.0
	Low	59	29.5
	Very low	25	12.5
Women's feeling about not recalling delivery details	Very good	54	27.0
	Good	78	39.0
	Average	59	29.5
	Bad	6	3.0
	Very bad	1	0.5
Overall satisfaction with the use of midazolam in labor	Very high	99	49.5

Variable	Mean (SD)		
	High	78	39
	Average	15	7.5
	Low	6	3.0
	Very low	2	1.0

Variables Affecting Women's Reasons for Choosing Midazolam

Table 5 shows the variables that influenced women's reasons. Older women, women with a lower BMI (25–30Kg/m^2), and women who had knowledge from previous use were more likely to request midazolam for pain relief.

Table 5: Variables related to reasons for choosing midazolam in the third stage, as part of the multinominal regression model

Variable	X^2	df	*p*-value
Age	9.4	2	.009
Educational achievement	10.4	6	.109
Body mass index	21.6	4	.000
Parity	22.3	8	.004
Baby gender known before delivery	3.3	2	.193
Source of information about midazolam	18.9	10	.041
Recommendation of the source of information	7.0	2	.030
Woman's attitude toward the use of midazolam	12.2	6	.057
Woman's awareness of complications of midazolam use	6.8	2	.034
Reason for not choosing to have an epidural analgesia	7.4	8	.490

Satisfaction with the Use of Midazolam

Both a VAS and LS were highly correlated in their measure of satisfaction and their relationship was monotonic (Kendall's tau-b correlation coefficient = 0.895), and the correlation was significant ($p<0.001$). The factors that correlated positively with higher satisfaction included having a baby boy, a positive feeling (good, very good) about not recalling delivery details, a positive attitude (agree, strongly agree) toward the use of midazolam, a positive reaction (good, very good) if refused midazolam, and reasons for not choosing an epidural (Table 6).

Table 6: Women's satisfaction with the use of midazolam as measured by VAS and LS

	Visual Analogue Scale			Likert Scale		
Variables	X^2	df	*p*-value	X^2	df	*p*-value
Age	4.40	2	.111	4.40	2	.111
Smoking	2.92	1	.088	2.91	1	.088
Educational achievement	5.89	3	.117	5.89	3	.117
Feeling about not recalling delivery details	23.30	4	.000	23.30	4	.000
Attitude toward use of midazolam	6.80	2	.033	6.82	2	.033
Awareness of midazolam complications	0.94	1	.333	0.94	1	.333
Reaction if denied midazolam	14.59	4	.006	14.60	4	.006
Reasons for not choosing epidural	14.43	4	.006	14.43	4	.006

DISCUSSION

Our results showed that the majority of the recruited women were knowledgeable about this particular use of midazolam. Their sources of knowledge included use in previous deliveries, friends or relatives, healthcare workers, and social media. Similar sources of medical information were shown by Dalhaug et al. [15]. They also showed that labor pain was one of the most commonly searched topics.

While seeking medical information from healthcare workers is reasonable, seeking information from the internet raises concerns not only about the quality of information but also about the impact of misinformation [16]. We acknowledge that we did not ask the women who gained their knowledge from a previous use where they gained the original knowledge before the first use.

The variables that influenced women's reasons for choosing midazolam included age, parity, source of information about midazolam, the source recommendation, and women's awareness of its complications. Our results showed that 88.5% of the recruited women were multiparous. This high percentage of multiparous women compared to primigravidae is related to our inclusion criteria, as women were required to have some knowledge about midazolam. This was supported by our finding that over 75% of the women gained their knowledge from previous use. Furthermore, 74% chose to have midazolam for the relief of pain associated with the delivery of the fetal head. While midazolam does not have an analgesic effect, the perception of women that it is a pain killer may be related to its retrograde amnestic properties [9]. This may reflect insufficient antenatal education about intrapartum pain management. Furthermore, 15% of the recruited women chose midazolam because of the fear of the delivery of the fetal head. Sitras et al. [17] showed that the fear of delivery was significantly associated with the use of epidural analgesia. We argue that women who choose to have midazolam because of the fear of the delivery of the fetal head may have a mild degree of tokophobia. A recent systematic review showed that, while there was a lack of clear operational definition for tokophobia, the prevalence was 14% [18]. We acknowledge that we did not study tokophobia as a separate entity in this report.

The results showed that around two thirds of the recruited women would feel bad or very bad if midazolam were declined in this delivery. This showed the importance of midazolam as a choice for some laboring women. Additionally, women who did not get their choice of analgesia in labor were more likely to have a negative recall of the delivery experience [19]. It is therefore important that pregnant women should be offered an opportunity to discuss their values, expectations, and preferences as this may affect their choices of pain relief in labor [20].

Regarding the reasons why women did not choose epidural analgesia, almost half of the recruited women chose fear of the procedure and its potential complication. Other reasons included financial limitations and previous poor experiences. A similar pattern of barriers against the use of neuroaxial analgesia was reported by Kranke et al. [21]. This reflects knowledge limitations about epidurals in our cohort.

Almost all women in our study were observed for up to 90 minutes after administration, and 8% developed hyperactivity/ agitations. All the side/ paradoxical effects resolved spontaneously during the observation period and none required an antidote administration. Another report showed that the rate of midazolam induced agitation/ hyperactivity is around 1% and the rate is more in patients of younger ages, with psychological conditions, among alcohol drinkers [22], and with higher infusion rates [23]. While none of the women in our cohort were alcohol consumers or had a known psychological/ psychiatric illness (this was an exclusion criterion), the apparently high rate in our cohort may be explained by the small sample size, undiagnosed psychiatric illness, or uncertainties concerning whether midazolam was administered at the same rate in all women. For safety reasons, the IV administration of midazolam should be supervised by healthcare workers skilled in maintaining airways with the availability of resuscitative drugs and equipment. Additionally, women should be continuously monitored for the early detection of complications such as hypoventilation or apnea, and the antidote (flumazenil 0.2 mg IV over 15–30 seconds) should be available [24].

Because of the sedation and hypnosis induced by midazolam, none of the women in our cohort were able to have skin to skin

contact. Vamour et al. [25] showed that maternal drowsiness was associated with an interruption of SSC, and this was probably the reason why none of the women in our cohort were able to initiate breast feeding within one hour of delivery, as recommended by the World Health Organization [26].

On the day after delivery, the women were asked how much they recalled of the delivery details. The results showed that almost half of them had low levels of recall. Carter et al. [27] showed that at short-term follow-up less than 72 hours after delivery, mothers may not be able to recall many peripartum details effectively. In their report, they studied the impact of administering opioids on the level of recall. This means that opioids may not be the only reason for not recalling delivery details. Additionally, our results also showed that around two thirds of the women felt good about not recalling the delivery details, which is supposed to be a positive experience, as shown by Karlström et al. [28]. We believe the good feeling women experienced is related to their reasons for choosing midazolam, which included a desire to forget delivery details. We acknowledge that we did not study why some women did not want to recall delivery details.

Almost 90% of the women were highly satisfied with the use of midazolam, and the factors that correlate with the satisfaction levels included the mothers' positive feelings about not recalling delivery details, having a positive attitude toward the use of midazolam, having a positive reaction if denied midazolam, and the reasons why they did not choose an epidural (Table 6). From the results, it seems logical that mothers who could not recall delivery details, or who avoided the fear or anxiety of an epidural were more likely to report higher satisfaction. This similar pattern of high satisfaction was reported with the use of an epidural, as shown by Tan et al. [29]. Their results showed that 68% of women were 'satisfied' or 'very satisfied' with an epidural. Furthermore, the use of Entonox for pain relief in labor has been associated with a high satisfaction rate [30]. This is probably due not only to pain relief but also to less anxiety during labor, which is associated with Entonox use [31].

We acknowledge the limitations of our exploratory study as being based in a single center and having a small sample; however, it is the first attempt to explore this particular use of midazolam. Additionally, the reasons why some women choose not to recall delivery details is worth studying from a psychological point of view.

CONCLUSION

The reasons why women chose to have midazolam in the third stage of labor were pain relief, fear of delivery of the fetal head, and the desire to forget delivery details. This reflects deficiencies in antenatal counselling for pain management in labor and the presence of barriers against the use of epidural analgesia, in addition to possible undiagnosed maternal anxieties. The high maternal satisfaction may make midazolam an option to consider in women who have tokophobia.

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Conflict of interest

The authors declare that they have no conflict of interest.

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لماذا تستخدم النساء الميدازولام في المرحلة الثالثة من المخاض؟ دراسة استكشافية

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الملخص

الهدف من الدراسة: يتم استخدام الميدازولام في المرحلة الثالثة من المخاض والولادة بعد ولادة رأس الجنين لأسباب مختلفة. وفي هذا التقرير تم تقييم أسباب موافقة النساء المشتركات على تلقي دواء الميدازولام في الوريد في المرحلة الثالثة من المخاض مباشرة بعد ولادة رأس الجنين بالاضافة الى مدى معرفتهن ورضاهن عن ذلك.

منهجية البحث: دراسة استكشافية مستقبلية في الفترة ما بين 2019/11/1 إلى 2020/11/1 في جناح الولادة في المستشفى التخصصي في عمان، الأردن. كانت أعمار المشاركات 18 عامًا أو أكثر، في حالة المخاض أو تحريض المخاض. تم تسجيل أسباب الموافقة والمعرفة، والتصورات، والشعور بالرضا. وبعد ذلك حللنا النتائج.

النتائج: تم تجنيد مائتي امرأة متوسط أعمارهن 29.4 سنة. أظهرت النتائج أن 88.5٪ من نساء كن من متعددات الولادة، و 61٪ لديهن بعض المعرفة حولعلاج الميدازولام، و 75.5٪ اكتسبن معرفتهن من خبرتهن في الولادات السابقة. كانت أسباب اختيار تناول الميدازولام هي تخفيف الام المخاض والخوف من ولادة رأس الجنين والرغبة في نسيان تفاصيل الولادة بنسبة 74٪ و 15٪ و 11٪ على التوالي. تضمنت العوامل التي ارتبطت بشكل إيجابي بأسباب النساء لاختيار الميدازولام سنًا أصغر، وعدد ولادات سابقة أعلى والخبرة المكتسبة في الولادات السابقة (جميع قيم ف <0.05). كان الشعور بالرضا مرتفعاعند 88.5٪ من النساء وارتبط ذلك مع عدم تذكر تفاصيل الولادة والتفاعل الإيجابي تجاه استخدام الميدازولام.

الاستنتاج: اختارت النساء تناول الميدازولام لتخفيف الآلام المصاحبة لولادة رأس الجنين أو الخوف من ولادة رأس الجنين أو الرغبة في نسيان تفاصيل الولادة. هذا يعكس أوجه القصور في فترة رعاية الحمل من حيث مناقشة موضوع الألم خلال المخاض والخيارات المتاحة للتعامل معه ووجود حواجز ضد استخدام المسكنات فوق الجافية.

الكلمات الدالة: آلام المخاض والولادة، المرحلة الثالثة من المخاض، مسكنات الألم خلال المخاض والولادة، الميدازولام، الشعور بالرضا.