Accepted: 4 January 2017

DOI: 10.1111/ger.12262

ORIGINAL ARTICLE

WILEY Gerodontology

# Sedation with orally administered midazolam in elderly dental patients with major neurocognitive disorder

Lena Rignell[1] | Mona Mikati[1] | Madeleine Wertsén[1,2] | Catharina Hägglin[2,3]

[1]Clinic of Pedodontics and Special Dental Care, Sahlgrenska University Hospital, Mölndal, Sweden

[2]Department of Gerodontology, Public Dental Service, Region Västra Götaland, Sweden

[3]Department of Behavioural & Community Dentistry, Institute of Odontology, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

**Correspondence**
Lena Rignell, Clinic of Pedodontics and Special Dental Care, SU/Mölndal, Mölndal, Sweden.
Email: lena.rignell@vgregion.se

**Funding information**
Local Research and Development Board for Gothenburg and Södra Bohuslän.

**Objective:** The aim of this study was to evaluate acceptance of treatment after oral sedation with midazolam in dental patients with major neurocognitive disorder.

**Background:** Midazolam is commonly used as premedication in paediatric dentistry, oral surgery and people suffering from dental fear. Little is known about its use in other patient groups.

**Methods:** Dental and sedation records of 61 patients (64% women) sedated with midazolam were examined retrospectively. All records came from patients with major neurocognitive disorder who had been referred to a special dental care unit in Sweden due to uncooperative behaviour and sedated with orally administered midazolam between 2006 and 2011. Data concerning dose, degree of acceptance of dental treatment (four-point scale) and number of possible interacting drugs were collected from dental records.

**Results:** On average, the participants were 80 years old (range: 62-93) and used 3.4 possible interacting drugs. The average midazolam dose was 0.11 mg/kg body weight, which is in line with the regional medical guidelines for sedation. Twenty-seven participants (44%) had no cooperation problems when sedated, twenty-six (43%) were treated with minor adaptations, five had poor cooperation, and three were not possible to treat. No statistically significant differences were found for degree of acceptance of treatment and dose or number of possible interacting drugs. Antiepileptics were used by 13% (n=7) with *good* or *quite good* acceptance compared to 37% (n=3) among those with *poor* or *no* acceptance. Unfavourable side effects were rare; one participant became hyperactive and one drowsier than expected.

**Conclusion:** Sedation with orally administered midazolam seems to be effective and safe in dental treatment of uncooperative persons with major neurocognitive disorder.

KEYWORDS
dementia, dental care, midazolam, neurocognitive disorder, sedation

## 1 | INTRODUCTION

Sedation with midazolam is commonly used as premedication in paediatric dentistry, oral surgery and people suffering from dental fear. However, little is known about its use in other patient groups, such as persons with major neurocognitive disorders.

Major neurocognitive disorder, formerly called dementia,[1] is not a specific disease. It is an overall term covering a wide range of cognitive

limitative symptoms such as decline of memory and reduced capacity to perform everyday activities. The reversible types are caused by, for example, depression, stroke and traumatic brain injuries. The most common progressive and irreversible types are Alzheimer's disease, vascular neurocognitive disorder, frontotemporal neurocognitive disorder and neurocognitive disorder with Lewy bodies. Cognitive disorder is an active area of research, but although symptom-relieving medication is available, there is currently no cure or medication that stops the disease progression.

The Swedish population is ageing, and people maintain their teeth to an older age.[2,3] Subsequently, there is an increasing group of elders with poor general health and a need for continuous preventive dental care. As with other activities of daily living, a person suffering from major neurocognitive disorder is usually not capable of taking care of their own oral hygiene.[4,5] In addition, persons with major neurocognitive disorder have a higher risk of caries, which further increases the need for dental care and preventive treatment on a regular basis.[6,7]

Patients with major neurocognitive disorder can be difficult to treat in dental care due to communication difficulties and lack of cooperation.[8] Sedation with nitrous oxide or benzodiazepines can facilitate dental treatment by improving cooperation and reducing stress during dental care.[9] However, a certain level of cooperation from the patient is still needed, when using nitrous oxide, which may not be possible in individuals with neurocognitive disorder.

Like nitrous oxide, benzodiazepines keep the patient sedated, but conscious. Unlike nitrous oxide, however, they require only a minimum of cooperation from the patient. There are several available benzodiazepines including midazolam, oxazepam and diazepam. Among these, midazolam has several advantages. It has a more rapid onset and a shorter half-life compared to other benzodiazepines[10]; both of these factors decrease the risk of falling before and after the sessions, which is a particular advantage for frail and old people. The only drawback of the short half-life is that treatment duration exceeding an hour may be problematic.

There are several ways to administer midazolam, including intravenous, nasal, rectal and oral administration.[11-16] Sweden has a tradition of administering midazolam orally at the dental clinic, especially in children, and all dentists are formally allowed to do this. This type of sedation has been used since the 1990s, and it is well-studied in paediatric dentistry[17-19] and among healthy adults before oral surgery.[20,21] However, in adult patients with impaired health, only a few case studies have been published.[22]

Older people commonly have extensive medication.[23] It is important to take this into consideration before sedation, as some drugs interact with midazolam and may prolong, reduce or enhance its effect. Prolonged or enhanced effect can be caused by Ca-antagonists, erythromycin, fluconazole, some retroviral drugs for HIV and grapefruit. Reduced effect is associated with certain antiepileptic drugs, such as carbamazepine, and antibiotics such as rifampicin.[24,25]

The aim of this study was to evaluate acceptance of treatment after orally administered midazolam in individuals suffering from major neurocognitive disorder, in relation to age, gender, weight, dose, interacting drugs, type of dental treatment performed and administration on multiple occasions. In addition, the occurrence of unfavourable side effects was examined.

## 2 | MATERIAL AND METHODS

In this retrospective study, dental and sedation records were examined regarding sedation with midazolam.

### 2.1 | Participants and caregivers

A total of 61 nursing home residents, with major neurocognitive disorder, sedated with orally administered midazolam during 2006-2011, were included retrospectively and consecutively. The participants had been referred to the clinic due to poor cooperation and/or a high level of anxiety. At the first visit to the clinic, an examination was planned, and if the participant was considered to be uncooperative, then sedation was offered for the following session. In some cases, such as when the participant had poor health status or heavy use of medication, an anaesthesiologist or the physician in charge was consulted regarding the suitability of using midazolam. Information about the sedation and treatment plan was given to relatives or nursing staff.

All dentists (n=7) who worked at the clinic during the study period were involved in the study.

### 2.2 | Procedure

In 1998, the dentists at the special dental care unit and physicians at the day surgery unit at Sahlgrenska University Hospital, Mölndal, developed guidelines for orally administered midazolam in dental treatment of adults. A separate sedation record was created to register the weight, age, and medical status[26] of the participant and hence determine the dose given.

Sedation was performed in accordance with the following guidelines.

<65 years: 0.2 mg/kg body weight.

>65 years: 0.1-0.15 mg/kg body weight.

The guidelines recommended waiting at least 20 minutes before starting treatment. A few participants who did not show any effect after more than 20 minutes were given another dose of half the initial amount.

All staff were regularly trained in cardiopulmonary resuscitation, and the antidote Lanexat was available at the clinic in case of emergency.

The dentist calculated the dose, gave it to the participant and checked that it was swallowed. In some rare cases the drug was administered with the help of a syringe in the back of the mouth (n=3), through a percutaneous endoscopic gastrostomy (PEG) tube (n=1), or in lemonade (n=1). After administration, the participant was kept under surveillance and a pulse oximeter was used to measure oxygen saturation. Dental treatment included examinations, X-rays, extractions, fillings, root canal treatment, prosthodontics and preventive care. Each treatment session was noted in the sedation record, including

documentation of medical history, current medication, dose of midazolam, duration of treatment and acceptance of treatment. After treatment, each participant was kept under surveillance in the clinic until at least 1.5 hours after administration of the drug.

## 2.3 | Scale of acceptance

The treating dentist evaluated the participants' acceptance of treatment according to a modified scale previously described by Carlsson, Linde and Öhman.[27] In order to coordinate the use of the different grades, the dentists, treating the patients with midazolam, were given an introduction to the scale. No other formal calibration was performed.

1. Treatment proceeded with no problems—acceptance: *good*
2. Minor adaptions made due to reactions from the participant, but all planned treatment was possible to accomplish—acceptance: *quite good*
3. Major problems occurred, requiring modification of the planned treatment—acceptance: *poor*
4. No treatment possible—acceptance: *none*

The Ethics Committee of the University of Gothenburg approved the study (ref: 879-14).

## 2.4 | Data collection

Data were collected by compiling information from the separate sedation records and the regular dental records, concerning age, sex, weight, medical history, reason for sedation, medication, dose of midazolam, treatment performed, and duration and acceptability of treatment. Other drugs were counted in number and grouped at the 2nd level according to the World Health Organization's Anatomical Therapeutic Chemical (ATC) classification system.[28] Drugs belonging to the groups N02-N07 and C08 (calcium antagonists) were recorded as possible interacting. Other drugs that can interact are erythromycin, fluconazole and some retroviral drugs for HIV, but no such drugs were used by the participants.

## 2.5 | Statistical analyses

Both parametric and nonparametric methods were used in the statistical inference testing. For continuous variables, Student's *t*-test was used for comparison between two groups (male vs female sex), and the one-way between groups ANOVA was used for comparison between four groups (grade of treatment acceptance). Tukey's HSD test was applied for post hoc comparison, and Fisher's exact test was used for comparison of proportions between groups (acceptance in relation to sex). Changes over time were analysed with the Wilcoxon signed-rank test (acceptance: sessions 1 and 2), Friedman's two-way ANOVA (acceptance: sessions 1, 2, and 3), and the one-way repeated ANOVA for continuous variables (dose: sessions 1, 2, and 3). The prechosen level of significance was $P<.05$ in all analyses. Version 21.0 of the SPSS software package was used for all statistical analyses.

# 3 | RESULTS

A total of 61 participants were included, all with neurocognitive disorder and referred to the special care unit. They comprised 39 women and 22 men, and had an average age of 80 years (range: 62-93; Table 1). Female participants were significantly older than male participants (82 years, SD=6.3 vs 75 years, SD=7.6; $P<.001$).

Twenty-seven participants (44%) had no cooperation problems after sedation with midazolam, and twenty-six (43%) could be treated with minor adaptation to arising reactions. Dental treatment was impossible only in three participants (5%; Table 2).

The average midazolam dose was 0.11 (0.06-0.21, SD=0.03) mg/kg of body weight (Table 1). Five participants (8%) received a lower dose (0.06-0.09 mg/kg) than the one recommended in the guidelines, and six (10%) a higher dose (0.16-0.2 mg/kg). Of the participants who received a lower dose, three received 0.09 mg/kg and one 0.08 mg/kg, while the participant with the lowest dose (0.06 mg/kg) was premedicated with oxazepam before leaving the nursing home. Acceptance of treatment was *good* or *quite good* in all but one of these low-dose participants. Among the six participants who received a higher dose, two were given an initial dose in accordance with the medical guidelines, but due to lack of sedative effect were given an additional dose of half the initial dose after 35 minutes. Acceptance of treatment was *good* or *quite good* for four of the high-dose participants, but *poor* or *none* for the two given an additional dose.

Statistically significant differences were found for age, sex and body weight in relation to degree of acceptance, with the largest variances mainly found for acceptance levels of *poor* and *none* (Table 2).

The average weight of the participants was 61.5 kg (SD=11.9) for the total group, 69 kg (SD=11.1) for the men and 58 kg (SD=10.9) for the women ($t=-3.8$, $P<.001$ for men vs women). The participants with poor acceptance of treatment (only women) had the lowest average weight and the non-treatable participants (only men) had the highest average weight (Table 2).

**TABLE 1** Gender, age, weight of the participants and mean dose midazolam given, number of interacting drugs and type of treatment

| **Participants (n=61)** | | |
|---|---|---|
| **Gender** | **n** | **%** |
| Male | 22 | 36.1 |
| Female | 39 | 63.9 |
| | **Mean** | **SD** |
| Age (y) | 79.8 | 7.6 |
| Weight (kg) | 61.5 | 11.9 |
| Dose (mg/kg) | 0.12 | 0.03 |
| N of interacting drugs | 3.4 | 2.0 |
| **Treatment:** | **n** | **%** |
| Examination, X-rays, prophylaxis | 13 | 19.7 |
| Fillings | 9 | 14.8 |
| Extraction/surgery | 38 | 63.9 |
| Prosthodontics | 1 | 1.6 |

**TABLE 2** Number of participants, gender, age, weight, dose, interacting drugs and type of treatment in relation to acceptance of treatment after sedation

| | | Acceptance | | | |
|---|---|---|---|---|---|
| | | Good | Quite good | Poor | None |
| Participants | n (%) | 27 (44.3) | 26 (42.6) | 5 (8.2) | 3 (4.9) |
| Gender[a]: | | | | | |
| Male | n (%) | 10 (44.3) | 9 (40.9) | – | 3 (13.6) |
| Female | n (%) | 17 (43.6) | 17 (43.6) | 5 (12.8) | – |
| Age (y)[b] | Mean SD) | 79.9 (8.2) | 79.8 (6.8) | 85.6 (2.4) | 69.0 (2.0) |
| Weight (kg)[c] | Mean (SD) | 64.1 (11.2) | 58.4 (12.0) | 54.4 (6.0) | 76.0 (9.5) |
| Dose (mg/kg)[d] | Mean (SD) | 0.11 (0.02) | 0.12 (0.03) | 0.13 (0.05) | 0.12 (0.06) |
| N of interacting drugs[e] | Mean (SD) | 2.7 (2.1) | 3.9 (1.8) | 4.4 (1.5) | 3.7 (1.2) |
| Treatment: | | | | | |
| Examination, X-rays, prophylaxis | n | 2 | 7 | 3 | 1 |
| Fillings | n | 4 | 5 | – | – |
| Extraction/surgery | n | 21 | 14 | 2 | 1 |
| Prosthodontics | n | – | – | 1 | – |

[a]$P$=.044; Fisher's exact test.
[b]$P$=.025; One-way ANOVA ($P$=.013, Poor>None; Tukey's HSD test).
[c]$P$=.023; One-way ANOVA ($P$=.05, Poor<None; Tukey's HSD test).
[d]$P$=.351; One-way ANOVA.
[e]$P$=.114; One-way ANOVA.

The participants used an average of 3.4 drugs (range: 0-8, SD=2.0) with a possible interaction with midazolam. No statistically significant difference was found for degree of treatment acceptance and number of interacting drugs (Table 2). Ten participants (16%) used antiepileptic drugs, which are considered to cause decreased or no effect in combination with midazolam. Of these ten participants, four had *good* acceptance, three *quite good*, one *poor* and two *none*. Thus, 13% of those with *good* or *quite good* acceptance used antiepileptic drugs compared to 37% with *poor* or *none* (Fisher's exact test, $P$=.115).

In the groups with *good* or *quite good* acceptance, treatment lasted 10-75 minutes (mean: 34 minutes, SD=11.8), while in those with *poor* or *none*, it lasted 15-50 minutes (mean: 27 minutes, SD=11.8).

The most common type of treatment given was extraction/oral surgery, followed by examination/prophylaxis/X-rays (Table 2).

Of the 61 participants, 42 had at least one additional session of treatment. Six of the eight participants who had *poor* or *no* acceptance at the first session (Table 1) were sedated a second time. At the second session, two remained *poor* and the other four improved to *quite good*. Two individuals who had *quite good* acceptance at the first session had *poor* acceptance the second time. In total, nine participants improved their acceptance of treatment between sessions 1 and 2, while five experienced poorer acceptance at session 2 ($z$=−1.4, $P$=.175).

Table 3 shows the 30 participants who were treated at least three times under sedation in relation to acceptance and dose. Nine of these improved their acceptance of treatment between sessions 1 and 3, while six saw a decline.

In the group of all sedations, unfavourable side effects were rare; one participant became hyperactive, and one drowsier than expected.

## 4 | DISCUSSION

The aim of this study was to systematically evaluate orally administered midazolam in dental treatment of persons with major neurocognitive disorder. Very little is known about premedication with this method in other patient groups, except within paediatric dentistry and oral surgery. According to the results of this study, orally administered midazolam seems to be an effective method when treating uncooperative patients with major neurocognitive disorder.

There are several ways to administer midazolam, including intravenous, nasal, rectal and oral administration. Studies concerning nasal and intravenous sedation with midazolam are far more common[11,12,16] than studies of oral sedation. In Sweden, intravenous sedation is rarely used in dentistry. Its advantages include fast onset and the opportunity to regulate the level of sedation, but it requires the ability to insert a venous catheter as well as continuous monitoring. Experience of nasal sedation with midazolam among Swedish dentists is limited. Intranasal midazolam has been shown to have a quicker onset and quicker recovery time for the patient compared to oral administration,[13] but side effects such as coughing and sneezing have been reported.[15] Rectal sedation is well functioning and commonly used in paediatric dentistry,[14] but is not an option for persons with neurocognitive disorder.

### 4.1 | Dose

The current guidelines were followed in calculating the doses of midazolam. Only two individuals had negative side effects such as increased drowsiness and hyperactivity. This low level of side effects and mainly good acceptance confirms the efficacy and safety of the

**TABLE 3** Participants (n=30) who received midazolam on at least three occasions, according to level of acceptance and dose (mg/kg of body weight) given

| | Acceptance[a] | | | | Dose [b] | |
|---|---|---|---|---|---|---|
| Treatment session | Good | Quite good | Poor | None | Mean | SD |
| 1 | 15 | 13 | – | 2 | 0.11 | 0.02 |
| 2 | 16 | 12 | 2 | – | 0.12 | 0.03 |
| 3 | 19 | 7 | 4 | – | 0.12 | 0.04 |

[a]*P*=.026; Friedman test.
[b]*P*=.155; One-way ANOVA.

guidelines. A lower dose than stated in the guidelines was given on five occasions. One participant with multiple illnesses was given a lower dose after consultation with an anaesthesiologist. This participant was later treated under general anaesthesia, due to lack of efficacy of sedation. In the other four cases, except for the participant premedicated with oxazepam at the nursing home, the participants received a dose just below the guidelines. On six occasions, the dose was exceeded. The reason in two cases was that acute surgery was required due to mobile bridges making food intake impossible. Two participants were given an additional dose after 35 minutes, but still displayed *poor* or *no* acceptance.

## 4.2 | Acceptability of treatment

Treatment acceptance was generally good, and the planned treatment could be completed in 90% of the cases. Among the 10% with unsatisfactory cooperation, five had poor acceptance and three were not affected by the drug at all. Of these, two of the men and one of the women were medicated with antiepileptic drugs, which may explain the outcome in these cases as antiepileptics can cause enzyme induction resulting in reduced or no effect.[24] Other explanations of poor acceptability require an in-depth analysis of other factors, such as type of neurocognitive disorder or daily condition, which were not included in this study. One observation is that there were only women in the group with poor acceptance and only men in the group with no effect. It is hard to believe that this result could be due to gender differences. Instead, a possible explanation could be that the men, being younger, heavier, and probably stronger, had more strength to react in the treatment situation than the frailer, older women.

The use of chemical restraints in uncooperative persons constitutes an ethical dilemma. These methods should be used on individual indications and in situations considered necessary for the patients continued well-being, such as in acute situations and for necessary preventive and restorative care. When faced with the need to use sedation to facilitate treatment, a thorough discussion with relatives and nursing staff should take place before the treatment, to inform these parties about the purpose of the sedation.

Half of the participants were treated on at least three different occasions, mainly with good results. Notably, two participants with initially *quite good* acceptance were treated a second time and then had *poor* acceptance, and six individuals whose initial acceptance was *none* or *poor* were treated a second time and four of them then had good cooperation. This might indicate that persons with neurocognitive disorder have better and worse days in terms of their condition, and it can be worthwhile to try again another time if treatment efforts initially fail.

On average, the participants consumed 3.4 other drugs with possible interaction with midazolam. No significant interactions were found, with the possible exception of antiepileptic drugs. However, to be able to draw any firm conclusions, further studies are required with larger groups of participants using antiepileptic drugs, thus giving higher power. Apart from antiepileptic drugs, many participants in this study were medicated with other psychiatric drugs. Given the risk of interaction, this could have resulted in an increased effect of midazolam, but we did not find this to be the case. The dose used for sedation was generally fairly low, which may be an explanation of why no interactions occurred.

## 4.3 | Dental treatment

During treatment involving extraction, 92% of the participants had *good* or *quite good* acceptance, while among participants who came for examination and prophylaxis 69% had *good* or *quite good* acceptance. This is the reverse of the result one might expect, namely that examination and prophylaxis would be more acceptable treatments than extraction. A likely explanation is that participants with the poorest cooperation did not get any treatment other than examination the first time midazolam was administered.

The short half-life of midazolam indicates that it may be difficult to accomplish prolonged treatments. However, in the present study, the treatments carried out for those with *good* or *quite good* acceptance lasted up to 75 minutes compared to up to 50 minutes among those with *poor* or *none*. It thus appears that treatment exceeding 60 minutes can be performed successfully, but it is essential to plan all procedures accurately to minimise the time used. The shorter treatment time among those with *poor* or *no* acceptance suggests that the lower level of acceptance was not connected to a prolonged treatment time caused by a reduced effect of midazolam, but was more likely associated with cooperation difficulties.

## 4.4 | Unfavourable side effects and risk

The intention of sedation with midazolam is a slight decrease in the level of consciousness. Protective reflex activities such as coughing and breathing should still be intact, but may be reduced. It is important to consider that people with neurocognitive disorder may already

have reduced pharyngeal reflex.[29] Even when sedated, the patient must be able to respond when spoken to and maintain clear airways. Previous studies have shown that unfavourable side effects such as respiratory depression, hyperactivity and drowsiness are rare,[22,30,31] and the findings in the present study bear this out. However, every sedation is a risk, and it is important for dental staff to have good knowledge of cardiopulmonary resuscitation and to be well aware of the procedures to be followed in case of an emergency situation. As a safety precaution, it is also recommended to use a pulse oximeter to monitor the patient's oxygen saturation, and oxygen should be available in case the patient becomes desaturated. Lanexat can be used as an antidote to midazolam if the patient becomes sedated more deeply than expected. In the present study, no such acute actions were required.

### 4.5 | Limitations

Neurocognitive disorder is an overarching term that describes a range of symptoms, such as memory problems and loss of intellectual abilities, which can result in difficulties in performing everyday activities. There are different types of neurocognitive disorders, including Alzheimer's disease, vascular neurocognitive disorder, neurocognitive disorder with Lewy bodies and frontotemporal neurocognitive disorder. The classification is based on what part of the brain is affected, and as a result, the symptoms can differ. It would have been preferable in the present study to register the different types of neurocognitive disorders. However, the medical records of the participants rarely mentioned the specific type.

The scale of acceptance was introduced to the dentists involved in treating patients with midazolam at the clinic, in order to coordinate the use of the different levels in the scale. All the dentists (n=7) who worked at the clinic during 2006-2011 were involved in treating the participants selected for this study. They were all experienced in special care dentistry, and all used to working with midazolam. As the study comprised a retrospective examination of dental records, it was not possible to perform any calibration regarding administration or patient care, which is a limitation of the study and may have influenced the assessment of acceptance. However, the results show that the medical guidelines were followed in terms of dose and medical assessment. In addition, we could not find any correlation between the treating operator and the acceptance. The eight participants with *poor* or *no* acceptance were treated by a total of five different dentists.

### 4.6 | Advantages

Patients in a special dental care unit are mainly adult persons unable to receive conventional treatment in a general dental practice due to cooperation difficulties. One such group is persons with major neurocognitive disorder. These individuals usually have a high risk of caries and require regular follow-ups.[7] Moreover, when sedation results in good or fairly good cooperation, this facilitates the dental treatment which in turn results in higher technical quality. Another advantage of midazolam is the short half-life, which allows patients to remain in the clinic during the recovery time, thus reducing the risk of falls and accidents at home and during transportation to and from the clinic. Even when acceptance of the treatment is poor, a brief examination is still often possible, and can provide a picture of whether further actions are necessary. The results of the present study clearly show that sedation with midazolam enables treatment in many patients with major neurocognitive disorder on a regular basis, likely meaning improved dental health in the long run.

## 5 | CONCLUSION

When midazolam was used as sedation, treatment acceptance was generally good and the planned treatment could be completed in most cases. Acceptance was not found to be dependent on dose, the type of dental treatment performed or interacting drugs. *Poor* and *no* acceptance were found among women with low weight and men with high weight. Unfavourable side effects were rare. The results indicate that *poor* or *no* acceptance at the first sedation does not rule out good cooperation the next time.

Sedation with orally administered midazolam thus seems to be effective and safe in dental treatment of uncooperative persons with major neurocognitive disorder.

## ACKNOWLEDGEMENTS

This study was supported by grants from the Local Research and Development Board for Gothenburg and Södra Bohuslän. The authors would like to express their sincere gratitude to Metha Brattwall, senior consultant and head of the day surgery unit at SU/Mölndal, for expert assistance in relation to questions about anaesthesia and sedation. We would also like to thank Kristina Skallsjö, Margit Gabrielson, Lotten Pihl and Janet Chi Johansson, who along with three of the authors treated the participants in the study.

## CONFLICT OF INTERESTS

The authors declare no conflict of interests.

## REFERENCES

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
2. Norderyd O, Koch G, Papias A, et al. Oral health of individuals aged 3-80 years in Jönköping, Sweden during 40 years (1973-2013). II. Review of clinical and radiographic findings. *Swed Dent J*. 2015;39:69–86.
3. Wennström A, Ahlqwist M, Stenman U, Björkelund C, Hakeberg M. Trends in tooth loss in relation to socio-economic status among Swedish women, aged 38 and 50 years: repeated cross-sectional surveys. 1968-2004. *BMC Oral Health*. 2013;13:63.
4. Hagman-Gustafsson ML, Holmen A, Strömberg E, Gabre P, Wårdh I. Who cares for the oral health of dependent elderly and disabled persons living at home? A qualitative study of case managers' knowledge, attitudes and initiatives. *Swed Dent J*. 2008;32:95–104.
5. Holmen A, Strömberg E, Hagman-Gustafsson ML, Wårdh I, Gabre P. Oral status in home-dwelling elderly dependent on moderate or substantial

supportive care for daily living: prevalence of edentulous subjects, caries and periodontal disease. *Gerodontology*. 2012;29:503–511.
6. Ghezzi EM, Ship JA. Dementia and oral health. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000;89:2–5.
7. Morishita S, Watanabe Y, Ohara Y, et al. Factors associated with older adults' need for oral hygiene management by dental professionals. *Geriatr Gerontol Int*. 2016;16:956–962.
8. Coenen M, Cabello M, Umlauf S, et al. Psychosocial difficulties from the perspective of persons with neuropsychiatric disorders. *Disabil Rehabil*. 2016;38:1134–1145.
9. Nicolas E, Lassauzay C. Interest of 50% nitrous oxide and oxygen premix sedation in gerodontology. *Clin Interv Aging*. 2009;4:67–72.
10. Reves JG, Fragen RJ, Vinik HR, Greenblatt DJ. Midazolam: pharmacology and uses. *Anesthesiology*. 1985;62:310–324.
11. Ransford NJ, Manley MC, Lewis DA, et al. Intranasal/intravenous sedation for the dental care of adults with severe disabilities: a multicentre prospective audit. *Br Dent J*. 2010;208:565–569.
12. Manley MC, Ransford NJ, Lewis DA, Thompson SA, Forbes M. Retrospective audit of the efficacy and safety of the combined intranasal/intravenous midazolam sedation technique for the dental treatment of adults with learning disability. *Br Dent J*. 2008;205:84–85.
13. Musani IE, Chandan NV. A comparison of the sedative effect of oral versus nasal midazolam combined with nitrous oxide in uncooperative children. *Eur Arch Paediatr Dent*. 2015;16:417–424.
14. Lindh-Strömberg U. Rectal administration of midazolam for conscious sedation of uncooperative children in need of dental treatment. *Swed Dent J*. 2001;25:105–111.
15. Wood M. The safety and efficacy of using a concentrated intranasal midazolam formulation for paediatric dental sedation. *SAAD Dig*. 2011;27:16–23.
16. Collado VFD, Nicolas E, Hennequin M. Conscious sedation procedures using intravenous midazolam for dental care in patients with different cognitive profiles: a prospective study of effectiveness and safety. *PLoS ONE*. 2013;8:e71240.
17. Erlandsson AL, Bäckman B, Stenström A, Stecksén-Blicks C. Conscious sedation by oral administration of midazolam in paediatric dental treatment. *Swed Dent J*. 2001;25:97–104.
18. Hartgraves PM, Primosch RE. An evaluation of oral and nasal midazolam for pediatric dental sedation. *ASDC J Dent Child*. 1994;61:175–181.
19. Day PFPA, Hibbert SA, Paterson SA. Effectiveness of oral midazolam for paediatric dental care: a retrospective study in two specialist centers. *Eur Arch Paediatr Dent*. 2006;7:228–235.
20. Rodrigo MR, Cheung LK. Oral midazolam sedation in third molar surgery. *Int J Oral Maxillofac Surg*. 1987;16:333–337.
21. Rune J, Eriksson L. Dosage of oral Midazolam in dentoalveolar surgery. *Tandläkartidningen*. 2001;93:40–42.
22. Boyle CA, Manley MC, Fleming GJ. Oral midazolam for adults with learning disabilities. *Dent Update*. 2000;27:190–192.
23. Hovstadius BHK, Åstrand B, Petersson G. Increasing polypharmacy – an individual-based study of the Swedish population 2005-2008. *BMC Clin Pharmacol*. 2010;10:16.
24. Magnusson MO. *Pharmacodynamics of enzyme induction and its consequences for substrate elimination*. 2007. Thesis, ISBN 978-91-554-6860-6 Available at: http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-7812. Accessed May 8, 2016.
25. Electronic Medicines Compendium (eMC). Midazolam. Available at: http://www.medicines.org.uk/emc/medicine/25538. Accessed May 12, 2016.
26. American Society of Anesthesiologists. ASA physical status classification system. Available at: https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system. Accessed February 18, 2016.
27. Carlsson SG, Linde A, Öhman A. Reduction of tension in fearful dental patients. *J Am Dent Assoc*. 1980;101:638–641.
28. WHO Collaborating Centre for Drugs Statistics Methodology. Guidelines for ATC classification and DDD assignment. 2015. Oslo, 2014. Available at: http://www.whocc.no/filearchive/publications/2016_guidelines_web.pdf. Accessed May 6th, 2016.
29. Easterling CS, Robbins E. Dementia and dysphagia. *Geriatr Nurs*. 2008;29:275–285.
30. McMillan CO, Spahr-Schopfer IA, Sikich N, Hartley E, Lerman J. Premedication of children with oral midazolam. *Can J Anaesth*. 1992;39:545–550.
31. O'Boyle CA, Harris D, Barry H, McCreary C, Bewley A, Fox E. Comparison of midazolam by mouth and diazepam i.v. in outpatient oral surgery. *Br J Anaesth*. 1987;59:746–754.

**How to cite this article:** Rignell L, Mikati M, Wertsén M, Hägglin C. Sedation with orally administered midazolam in elderly dental patients with major neurocognitive disorder. *Gerodontology*. 2017;34:299-305. https://doi.org/10.1111/ger.12262