FACULTEIT GENEESKUNDE
Departement Mondgezondheidswetenschappen
Dienst Tandheelkunde
Kinder- en Bijzondere Zorgverlening

Optimization of procedural sedation protocol for dental care delivery in adults with mental disability

Ine Opsomer
TSO3 Kinder- en Bijzondere Tandheelkunde
Academiejaar 2013-2014

Promotor: Prof. Dr. D. Declerck
Co-promotor: Elinor Bouvy

Acknowledgements

I would like to thank a few people who helped me with the realization of my master thesis:

My promoter professor Dominique Declerck and co-promoter Mrs Elinor Bouvy
for their help and counselling

My partner Bram for his patience, never ending support and unconditional love

My parents and brother for their endless support throughout my whole education

The managing board, the doctors, the nursing staff, the social workers and the caregivers of the nursing home Het Gielsbos for their willingness to help and their assistance during the study

Lie, my assistant, for her incredible support and everlasting optimism

Kathy Declerck for her help with the statistical analysis of the data

The residents of the nursing home Het Gielsbos for their smile, honesty, enthusiasm
and participation in the study

The parents and relatives of the residents of the nursing home Het Gielsbos for confiding in me and to let their beloved ones participate

And of course my aunt Linda, my biggest source of inspiration and most enthusiastic fan

Thank you so much!

Table of Contents

Figures and tables

Figures

Tables

Introduction

Oral health is essential for general health and quality of life. Studies suggest however that in people with mental disabilities oral healthcare is one of the most neglected parts of healthcare delivery[1].

In this particular population oral health can be compromised by the disability itself, indirectly by medication or as a consequence of limited access to oral healthcare[2].

In Belgium there are not many data available on the oral health of people with mental disability.

In 2010 a study investigated the objective need for and degree of dental treatment in adults with special needs through a clinical oral investigation in a convenience sample of 707 patients[3].

A healthy dentition, without missing or restored teeth, was seen in only 5% of the adults.

In 78% visible plaque was registered and in 68% calculus was present. In the majority of participants oral hygiene was thus scored as inadequate. However, proper oral hygiene is crucial in the prevention of periodontal diseases and caries lesions. Poor oral hygiene could be linked to suboptimal oral hygiene practices, lack of professional debridement, salivary characteristics or biofilm properties[3].

Visible caries lesions were noticed in 56% and 64% had lost teeth because of caries. The periodontal state was investigated using the Dutch Periodontal Screening Index (DPSI). Looking at the highest DPSI-score 19% of the adults got the score 'healthy', while in 26% the score 'bleeding after probing' was the highest individual score. In 23% presence of shallow pockets (4-5 mm) was recorded, while 3% of the adults had a pocket of more than 5mm. These data reflect higher disease levels when compared to those of the general Belgian population where 50% was diagnosed with gingivitis and 17% presented with pathological periodontal pockets. Erosion was found in 5%, abrasion in 9% and attrition in 34% of the adults. In 15% lesions or alterations of the soft tissues were diagnosed. One fourth of the adults with an edentulous maxilla and one third of the adults with an edentulous mandible had no prosthetic appliance. Also in adults with a partial edentulous maxilla and mandible the proportion without dental prostheses was high: 47% and 38% for the ones with 1 to 4 teeth and 53% and 63% for the group with 5 to 8 teeth present. Evaluation of the hygiene of the removable dentures revealed that plaque was present in 55% and calculus in 34%. Only in 2% of the investigated adults missing teeth were replaced by implants[3].

It can be concluded that people with a mental disability face the same type of oral diseases as their non-handicapped peers but with a higher prevalence[3-5]. They often show worse oral hygiene for which they are frequently depending on others, more and severe forms of periodontitis, comparable caries experience but more untreated caries lesions and less restored teeth[2]. Because their teeth are rather extracted than restored, they present with more missing teeth[6]. The prevalence of damage as a consequence of trauma, enamel defects, delayed eruption, persisting primary teeth and grinding is also higher[2].

Delivery of dental care in people with a mental disability is very demanding and presents many challenges. Among these are the limitations of the patient to cope with dental treatment. This necessitates in many cases treatment provision under general anesthesia, requiring treatment delivery in a hospital setting. As a consequence, minor dental interventions and regular preventive treatments are often postponed with negative impact on the quality of life and long-term (oral) health of the individual as a result[5].

An alternative is the use of procedural sedation. This technique has been widely used in 'Het Gielsbos', a nursing home for people with a mental disability. For many years already, patients in need of medicinal support for dental care delivery receive lorazepam or a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate. In recent scientific literature however, midazolam is put forward as the sedative of first choice for procedural sedation[7]. Main reasons for this are: prompt absorption of the drug, efficient transportation, rapid metabolization and short half-life. In addition, it is important that the procedural sedation of people with mental disability when receiving dental care can be applied in a safe way, based on sound indications and with high effectivity.

No other reports comparing different sedation protocols in this particular population could be retrieved. This study aims to assess whether the switch to a protocol using midazolam presents an improvement for patient care, i.e. allows regular dental care to be performed under at least the same conditions as with the existing protocol but with less discomfort for the patients (shorter effect) and without additional side-effects. This research can therefore contribute to the optimization of dental care delivery in this specific population.

Materials and Methods

Subjects

Participants were recruited among residents of 'Het Gielsbos'. This is a nursing home situated in Gierle, Belgium, where 287 people with a mental disability live today. Many of them have an intense need for care or need support in other areas. This support cannot be offered by the family in the home situation. Het Gielsbos is recognized for care delivery to children between 0 to 21 years old with a moderate to severe disability with or without motor, sensory, epileptic, behaviour or emotional disorders and adults with a moderate or severe mental disability who are not able to visit a sheltered workplace. In addition to a home environment and professional guidance het Gielsbos also offers a wide range of daytime activities and therapies. People with a mental disability who live at home or in neighbouring nursing homes can use some of the facilities offered. Het Gielsbos has 32 living groups and the number of residents per living group varies between 6 and 10 people.

Residents with minimum age of 18 years, residing at least 6 months in the nursing home and needing medicinal support for dental care were eligible for inclusion in the study. A medical contra-indication for use of one of the sedation protocols, as determined by the physician of the nursing home, was used as an exclusion criterion. Patients were included until the number of 20 patients per subgroup was reached.

Procedural sedation protocols

The existing procedural sedation protocols consist of oral administration of lorazepam (referred to as protocol B1) or a cocktail for intramuscular injection with a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (protocol B2). The newly introduced procedural sedation protocol consists of oral administration of midazolam (protocol A)[7-11]. The sedative was administered by the nurse of the facility, in the presence of a physician, between 45 and 60 minutes before the start of the scheduled dental treatment. In case of oral administration, the nurse made sure that the medication was completely swallowed by the patient. The physician and nurse who administered the medicine were the only persons having knowledge of which sedation protocol had been applied. Neither was involved in the evaluation of the outcomes. Standard medications or treatments were continued concurrently with the sedation protocol. In case of changes to the standard medication of the patient, this was mentioned explicitly in the patient file.

Table 1: Procedural sedation protocols[7-11]

	Medication	Administration route	Dose
A	Midazolam 5mg/ml (Dormicum®, Roche)	Oral route	15 mg, dissolved in apple juice
B1	Lorazepam 2.5mg (Temesta®, Pfizer)	Oral route	2.5mg (1 tablet)
B2	Diazepam 10mg/2ml (Valium®, Roche)	Solution for IM injection	10 mg
	Biperideenlactaat 5mg/1ml (Akineton®, Laboratorio Farmaceutico)	Solution for IM injection	5mg
	Dehydrobenzperidol 5mg/2ml (Dehydrobenzperidol®, Prostrakan)	Solution for IM injection	3.125mg/m^2 body surface
	Atropine sulfate 0.25mg/1ml (Atropine sulfate Sterop®, Laboratoria Sterop)	Solution for IM injection	0.25mg

Trial design

Patients eligible for participation to the study were included in subgroup 1 or 2, based on the sedative protocol they were receiving for dental care delivery before entering the study. The sequence of administration of both protocols was determined using a randomization table with sequences A-B1/B2 or B1/B2-A (Figure 1).

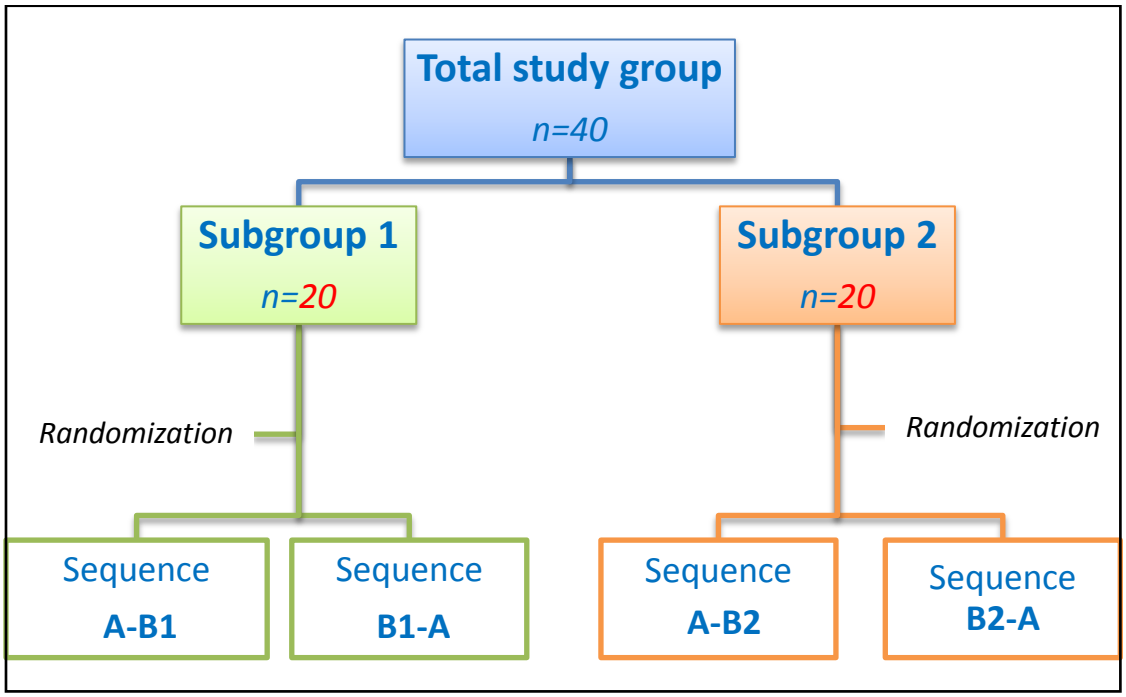


Figure 1: Randomization scheme

Dental treatment

In nursing home Het Gielsbos a fully equipped dental cabinet is available. The dental staff, which consists of a dentist specialized in special care delivery and a dental nurse, provides regular dental care to all of the residents. When residents come for a dental visit, they are accompanied by a supervisor. For the present study, the dental treatment delivered consisted at each treatment session of a complete oral investigation and dental prophylaxis using an ultrasonic cleaning device. The interval between the two treatment sessions ranged from 3 to 4 months.

Evaluation

The level of cooperation of the patient was scored, during and after dental treatment, independently by the dentist, the dental nurse and the supervisor of the patient using the scale described by Van Grunsven (Table 2)(Attachment 2)[12].

Patient safety was evaluated by monitoring of vital parameters and consisted of blood pressure, pulse and oxygen saturation recorded using a sphygmomanometer (SK Speidel & Keller, Primus Stabil 3) and a pulse oximeter (Siemens, MicroO2)[13]. Recordings were started before dental treatment and continued throughout dental treatment delivery, whenever the patient allowed this.

After dental treatment, the caregivers of the nursing home scored the comfort of the patient and any possible side-effects during 24 hours using a questionnaire. This questionnaire focused on several aspects of the behaviour and comfort of the patient such as appetite, toilet behaviour, level of consciousness and concentration, pattern of epileptic insults, mood changes, sleeping pattern and changes in level of motor skills. When evaluating comfort and behaviour, caregivers were asked to define the exact number of levels of change ranging from much worse to much better (Attachment 3).

Table 2: Scale of treatability as described by Van Grunsven[12] (1977)

IV Cooperative	- Good contact with the dentist, verbally or through gestures - Shows interest in what is happening - Lies relaxed in the chair - Is cooperative during the investigation as far as motor skills enable it
III Passive	- No contact - Not noticeably tensed in the chair - Permits several parts of the investigation passively - Needs to be helped with everything but there is no resistance
II Hesitating	- Very cautiously - Tries to delay the investigation - Needs to get used to the situation, but attempts to escape the treatment can be corrected
I Non-cooperative	- Verbal and/or physical signs of displeasure - Needs to be fixated in the chair - Calms down after a while but during the whole investigation periods of resistance
0 Untreatable	- Continuous resistance, which cannot be influenced within a period of 10 minutes

Ethical standards

The trial was conducted in compliance with the principles of the Declaration of Helsinki (2008), the principles of Good Clinical Practice and in accordance with all applicable regulatory requirements. The protocol and all related documents were submitted for review to the Federal Agency for Medicines and Health Products (FAMHP) for Clinical Trial Authorization and the relevant Ethics Committee (Commissie Medische Ethiek van Universitaire Ziekenhuizen KU Leuven).

Written informed consent was obtained from the subjects or their legal representatives. These informed consents were in accordance with the requirements of all applicable regulatory agencies and laws (Attachment 4).

Data management

Clinical as well as questionnaire data were entered into Excel files (Microsoft Office 2007) with data validation in order to minimize faulty input.

Statistical analyses

In order to be able to detect a 20% difference in level of patient cooperation with a confidence level set at 5%, it was calculated that 20 patients needed to be included in each subgroup, leading to a total of 40 study patients. Statistical analysis included all patients having received both sedative protocols. In case of incomplete data, a detailed analysis of reasons for missingness of data was performed.

The present report compiles data from interim analyses.

Results

Description of the study sample

The present report includes the results obtained in 23 patients (interim analyses). Based on the study set-up, 10 patients were included in group 1 (protocol B1) and 13 patients in group 2 (protocol B2) (Table 3).

In group B1 there were 4 men and 6 women, in group B2 8 patients were male and 5 patients female, yielding an overall gender distribution of 52% male and 48% female.

Following the randomization procedure, procedural sedation protocol A was administered for the first treatment session in 10 patients while in 13 cases this protocol was administered for the second dental treatment session (Table 3). The interval between these two sessions ranged from 3 to 4 months.

Table 3: Sample characteristics (gender and protocol sequence)

		Group B1		Group B2		Total	
		N	%	N	%	N	%
Gender	Male	4	40.0	8	61.5	12	52.2
	Female	6	60.0	5	38.5	11	47.8
Sequence	A-B	5	50.0	5	38.5	10	43.5
	B-A	5	50.0	8	61.5	13	56.5
TOTAL		10	100.0	13	100.0	23	100.0

A-B = first treatment protocol supported by protocol A and second by protocol B (1 or 2); B-A = first treatment session supported by protocol B (1 or 2) and second by protocol A

Table 4 describes sample characteristics according to age. Participants were between 16 and 59 years old with a mean of 46.8 years and a standard deviation of 12.5. In group B1 the age of the patients ranged from 16 to 59 years with a mean of 43.3 years and a standard deviation of 14.7. In group B2 the youngest patient was 25 years old while the oldest was 59 years. The mean age of this group was 49.5 years with a standard deviation of 10.3. Regarding the inclusion criteria residents of nursing home Het Gielsbos were only allowed to participate in the study when they were at least 18 years old. In concert one exception was made for a girl who was 16 years old at the moment of recruitment. Because of her mature posture and the fact that she always received medication with an adult dose it was decided to include her data in the analysis.

The body weight of the participants ranged from 45 to 84 kilograms with a mean of 64.7 kilograms and a standard deviation of 10.5. In group B1 the mean was 63.9 kilograms with a standard deviation of 12.3 and the body weight ranged from 48 kilograms to 84 kilograms. In group B2 the weight lied between 45 en 80 kilograms with a mean of 65.2 kilograms and a standard deviation of 9.4 (Table 4).

Table 4: Sample characteristics (age and body weight)

	Group B1		Group B2		Total	
	Mean (Range)	SD	Mean (Range)	SD	Mean (Range)	SD
Age	43.3 (16-59)	14.7	49.5 (25-59)	10.3	46.8 (16-59)	12.5
Body weight	63.9 (48-84)	12.3	65.2 (45-80)	9.4	64.7 (45-84)	10.5

Level of cooperation during dental treatment

The level of cooperation of the patient during dental treatment was scored independently by the dentist, the dental nurse and the supervisor who accompanied the patient during the treatment session, using the scale described by Van Grunsven[12].

Using procedural sedation protocol A, the dentist considered 17.4% of the patients as being untreatable whereas the dental nurse and the supervisors attributed this score in 8.7% and 17.4% of the cases respectively. In 34.8% of the treatment sessions the dentist scored the patient as non-cooperative. This was the case in 26.1% and 43.5% of the sessions from the point of view of the dental nurse and supervisor respectively. The percentage of the patients that were called hesitating was 21.7% according to the dentist and according to the dental nurse and the supervisor the percentages were 34.8% and 13.0% respectively. The patients were considered passive in 26.1% of the cases when looking at the scores given by the dentist, while 21.7% of the patients received these scores from the dental nurse and the supervisor. The dentist and the supervisors scored none of the patients as cooperative while the dental nurse gave the highest score of treatability in 8.7% of the patients. During one treatment session where procedural sedation protocol A was used, the supervisor of the patient was not present and therefore unable to evaluate the level of cooperation (missing value) (Figure 2).

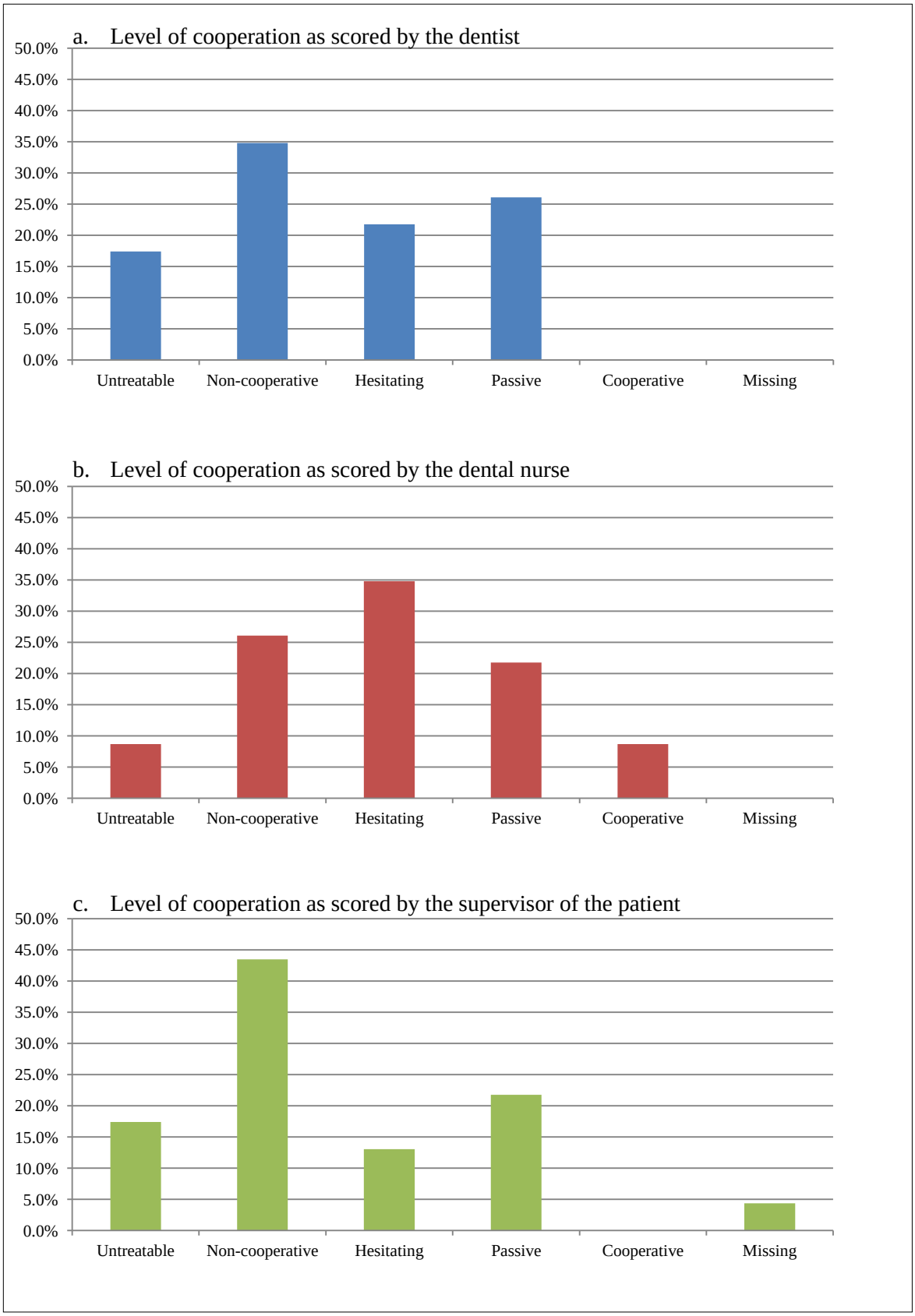
Figure 3 presents information on the level of cooperation when using protocol B1. While the dentist and supervisor scored most patients as non-cooperative (60.0% and 60.0% respectively), the dental nurse rated more patients as untreatable (40.0%) (Figure 3). For patients treated with protocol B2, scores tended overall more towards hesitating and passive, this for all scorers (Figure 4).

Table 5 summarizes the differences in cooperation level assessed at individual level. When comparing protocol A to protocol B1, the dentist, the dental nurse and the supervisor rated this protocol as comparable or better in 90.0% of the cases and in 66.7% of them the effect was considered as (at least slightly) better (Table 5 and Figure 5a). When only the scores of the dentist were considered the effect was at least equal in 80.0% and better in 60.0% (Figure 6a).

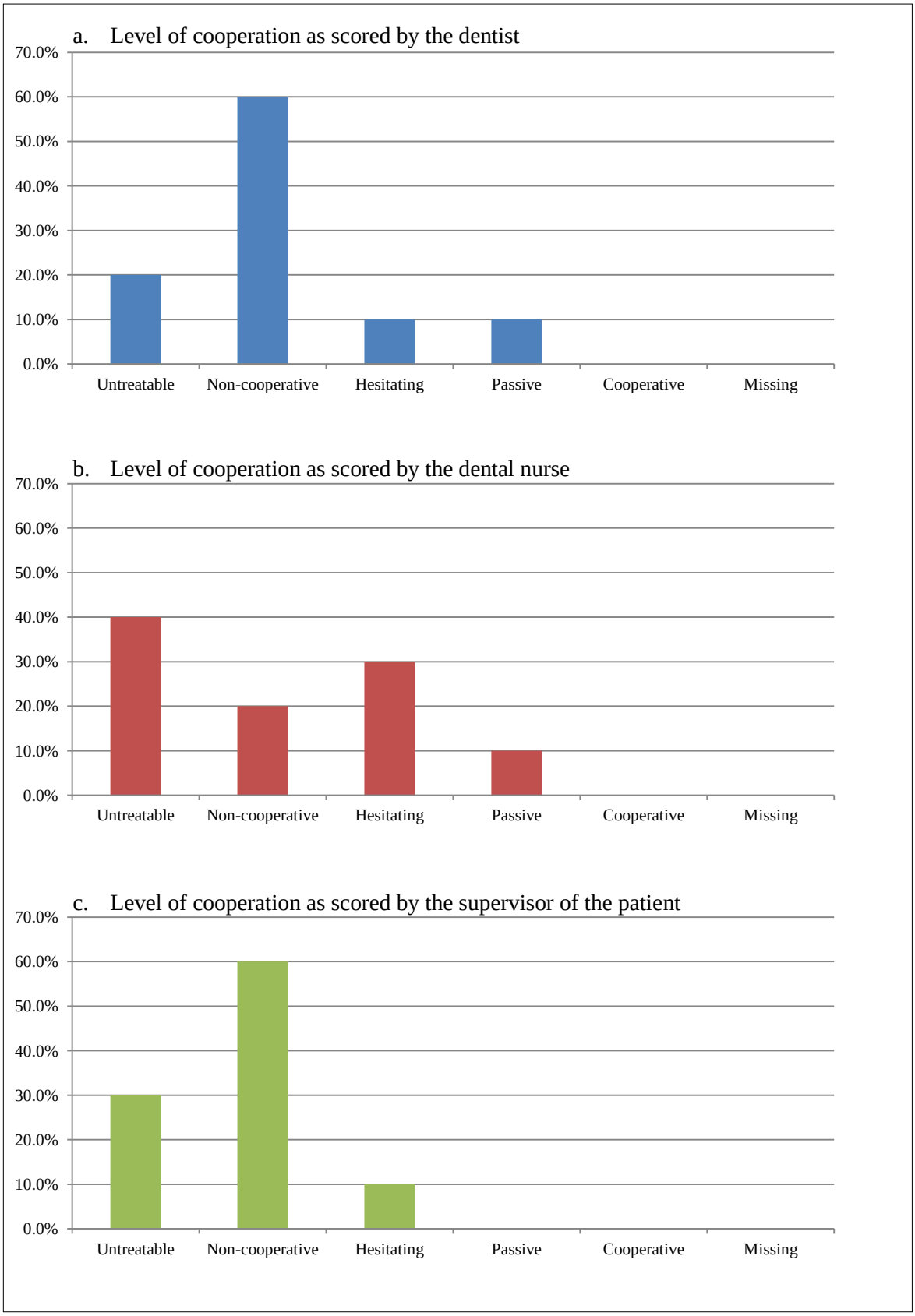
The scores of the dentist, dental nurse and the supervisor indicate that in comparison to protocol B2 the level of cooperation of the patient after administration of protocol A was equal or better in 52.6%

of the cases while in 28.9% of the subjects the cooperation was (at least slightly) better (Table 5 and Figure 5b).

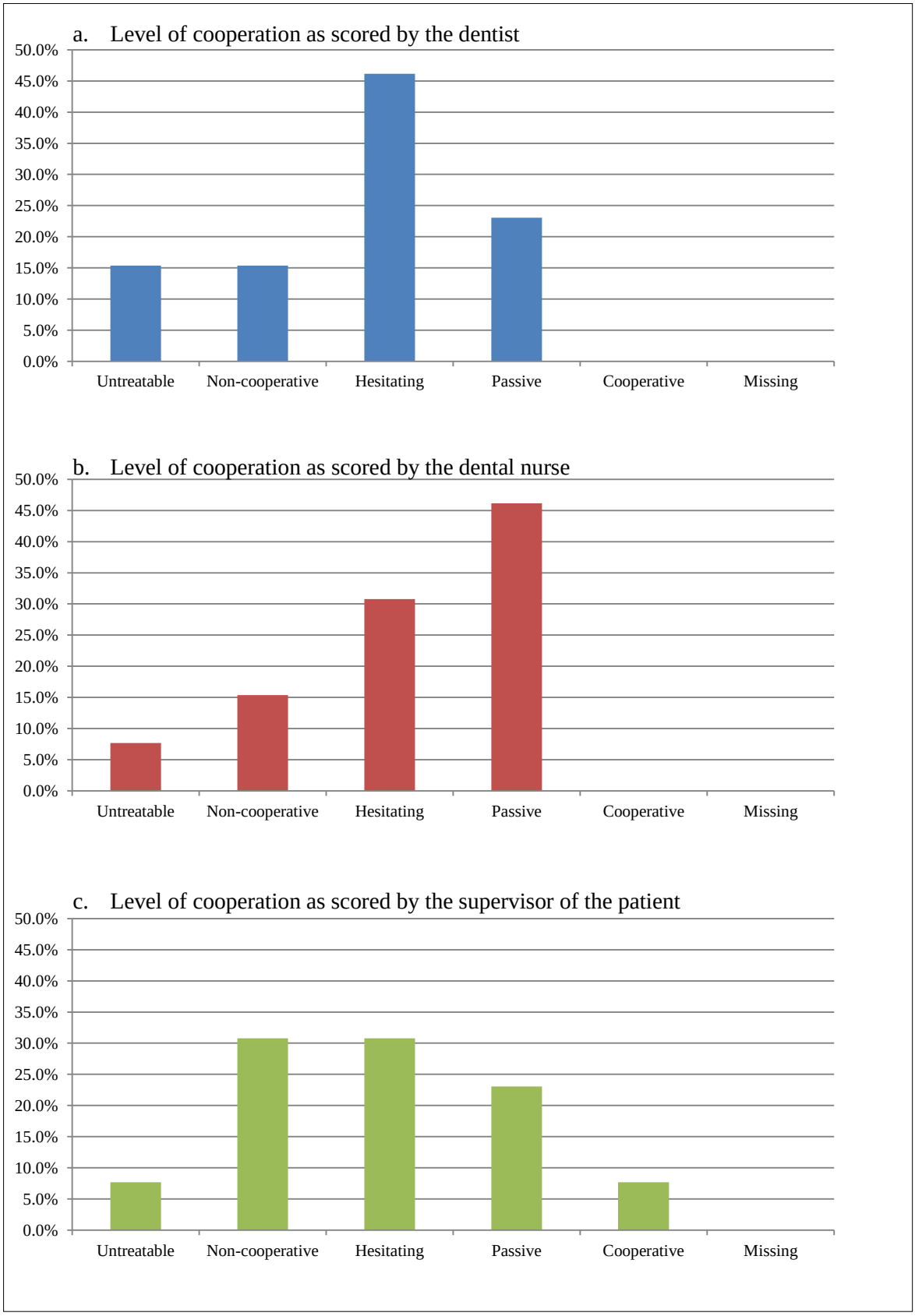
In 61.5% of the cases the dentist considered the level of cooperation as at least the same while in 30.8% the cooperation was evaluated as better when procedural sedation protocol A was administered (Figure 6a).



Figures 2 a, b and c: Distribution of level of cooperation using protocol A as scored by dentist (a), dental nurse (b) and supervisor (c) (N= 23 patients)



Figures 3 a, b and c: Distribution of level of cooperation using protocol B1 as scored by dentist (a), dental nurse (b) and supervisor (c) (N= 10 patients)



Figures 4 a, b and c: Distribution of level of cooperation using protocol B2 as scored by dentist (a), dental nurse (b) and supervisor (c) (N= 13 patients)

Table 5: Difference in level of cooperation using protocol A versus protocol B1 or B2 measured at individual patient level

	Protocol A versus protocol B1						Protocol A versus protocol B2					
	Score Dentist	Score Nurse	Score Supervisor	Total	CUM	CUM(%)	Score Dentist	Score Nurse	Score Supervisor	Total	CUM	CUM(%)
4 levels ↑	0	1	0	1	1	3.3	0	1	0	1	1	2.6
3 levels ↑	1	0	1	2	3	10.0	1	0	0	1	2	5.3
2 levels ↑	1	2	1	4	7	23.3	0	0	2	2	4	10.5
1 level↑	4	4	5	13	20	66.7	3	3	1	7	11	28.9
Idem	2	2	3	7	27	90.0	4	3	2	9	20	52.6
1 level ↓	1	1	0	2	29	96.7	2	2	3	7	27	71.1
2 levels ↓	1	0	0	1	30	100.0	1	2	2	5	32	84.2
3 levels ↓	0	0	0	0	30	100.0	2	2	1	5	37	97.4
4 levels↓	0	0	0	0	30	100.0	0	0	1	1	38	100.0
Missing	0	0	0	0			0	0	1	1		

This table shows the number of patients that scored a certain difference in level of cooperation using protocol A versus protocol B1 or B2 according to the dentist, the dental nurse and supervisor. The cumulative scores indicate the sum of the scores of all evaluators for this respective difference in level of cooperation and all the differences mentioned higher in exact number or percentage.

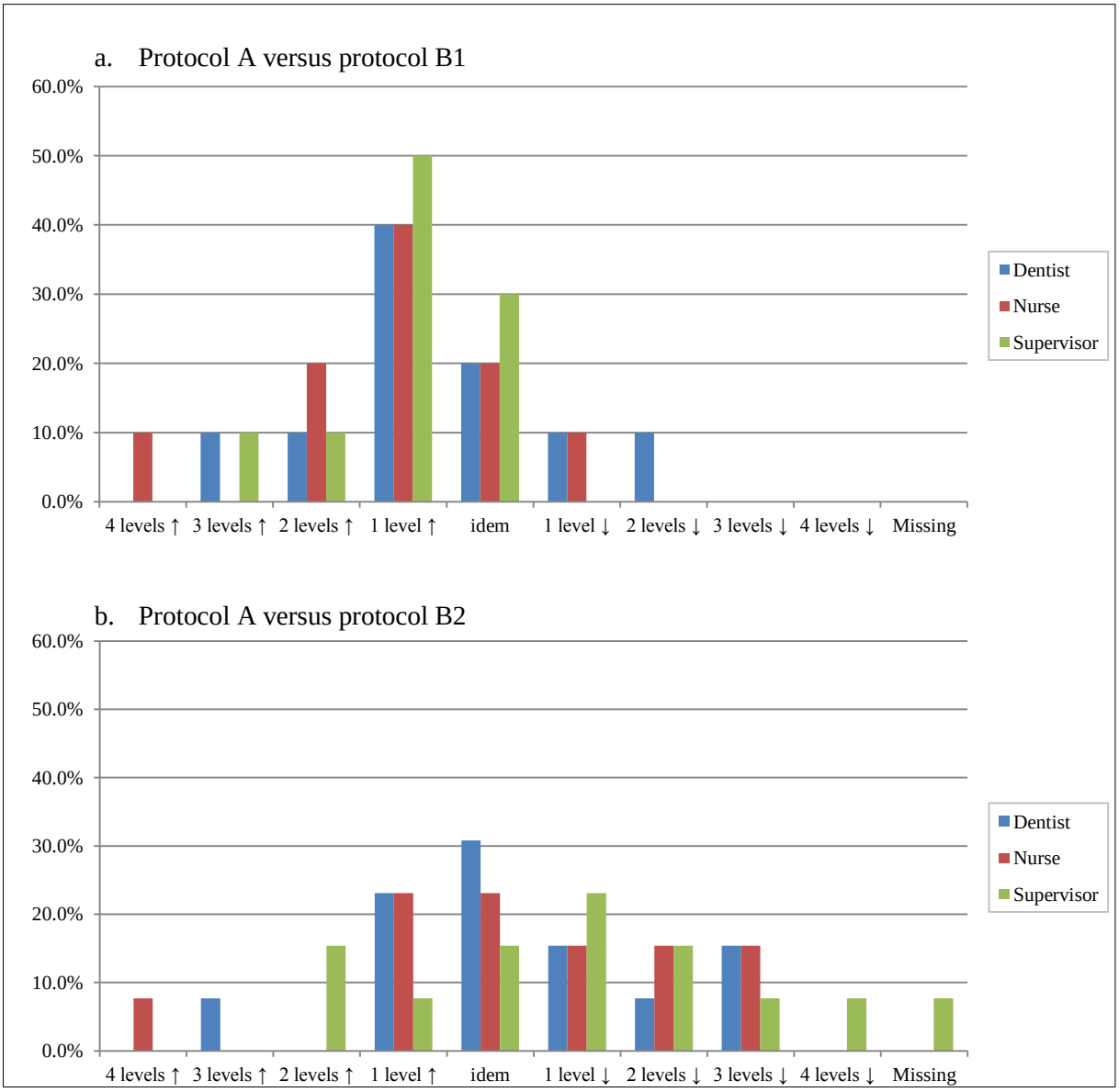
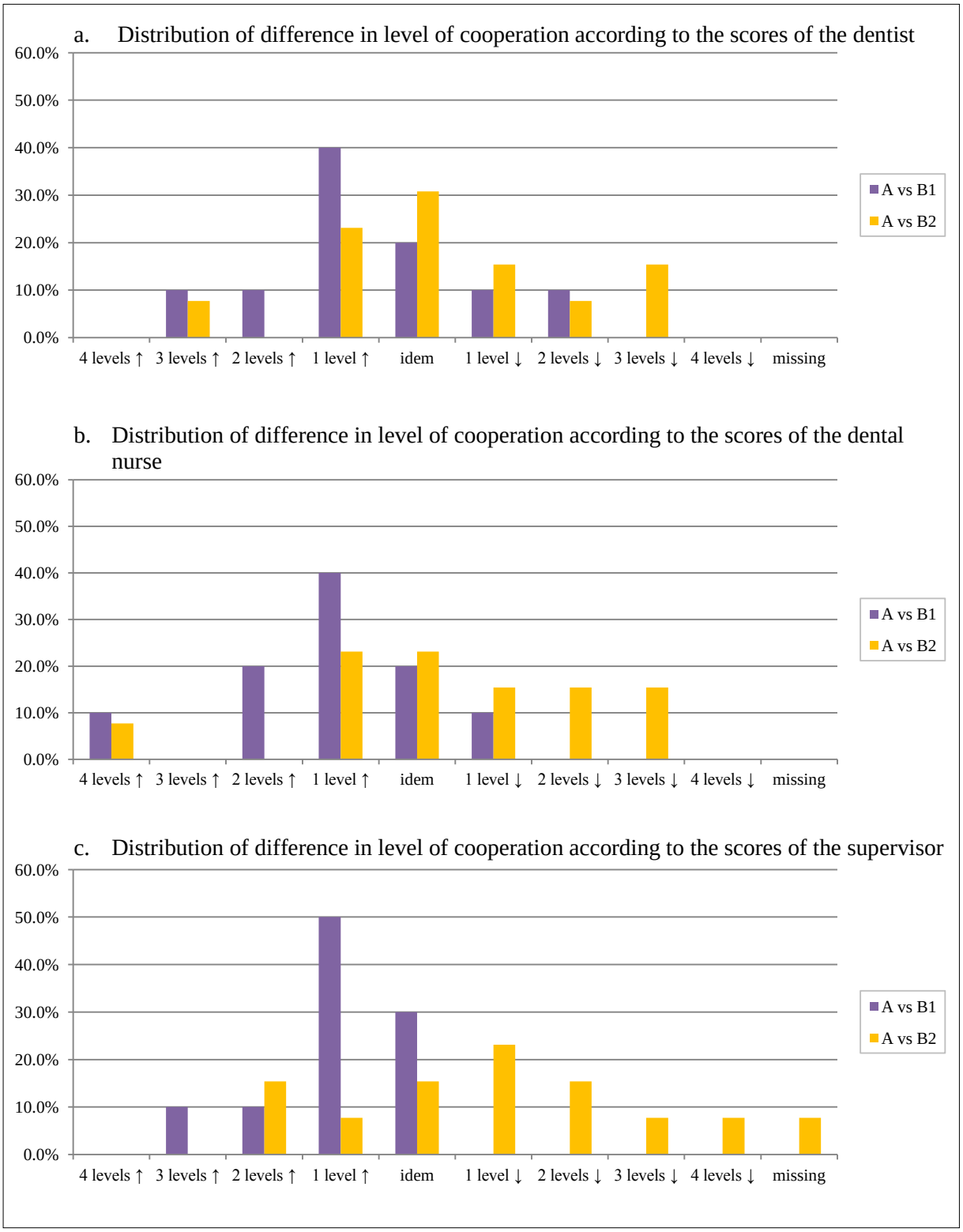


Figure 5: Distribution of difference in level of cooperation after administration of protocol A and B1 or B2 as recorded by dentist, dental nurse and supervisor



Figures 6 a, b and c: Distribution of difference in level of cooperation as scored by dentist (a), dental nurse (b) and supervisor (c): comparison of protocol A versus B1 and A versus B2

Patient comfort and side-effects

After dental treatment, the caregivers of the nursing home scored the level of comfort for the patient and any possible side-effects during 24 hours after administration of the procedural sedation protocol using a questionnaire. This questionnaire focused on several aspects of the behaviour and comfort of the patient such as appetite, toilet behaviour, level of consciousness and concentration, pattern of epileptic insults, mood changes, sleeping pattern and changes in level of motor skills. Figures 7 and 8 show the percentage of patients with equal or higher comfort level after administration of protocol A in comparison to protocol B1 or B2 at different points in time and for each aspect of comfort or behaviour that was assessed. The extent of change is indicated using colour coding.

Results show that protocol A had an equal or lower impact on appetite compared to both protocol B1 and protocol B2 in respectively 90.0% and 76.9% of the patients one hour after administration of the sedative. In one patient there was a difference in appetite reported 24 hours after administration and this in favour of protocol A when compared to protocol B2 (Figures 7a and 8a).

Protocol A had an equal or lower impact on toilet behaviour during the day in all the participants of group B1 with the exception of 1 patient 4 hours after administration (Figure 7b).

Fine motor skills were at the same level or less affected by protocol A versus B1 in 60.0% of the cases one hour after administration, and in 90.0% of patients 4 and 8 hours after administration (Figure 7d). When compared to protocol B2, the respective percentages were 46.2%, 69.2% and 76.9% (Figure 8d).

Comparable results were noted focusing on the impact on gross motor skills (Figures 7e and 8e). When comparing protocol A to protocol B1, in one patient a lower impact was reported 24 hours after administration of the sedative (Figure 7e).

The level of consciousness was equal or better in 50.0% of the patients 1 hour and 2 hours after administration of protocol A when compared to protocol B1. While the percentage of patients in which protocol A and B1 had a similar effect stayed the same at 4 hours, the number of patients in which the effect of protocol A was less pronounced rose from 10.0% to 50.0% (Figure 7f). In group B2 in 76.9% of the patients the impact of protocol A on the level of consciousness was equal or lower. This percentage rose to 84.6% 4 hours after administration of the sedative (Figure 8f). In both groups a slight decrease was noticed 8 hours after administration of protocol A in the number of patients in which this protocol had an equal or lower effect. In each group one patient had a lower effect on the level of consciousness 24 hours after administration of protocol A (Figures 7f and 8f).

Analysis of the effect of administration of the different protocols on the level of concentration shows that in 50.0% and 69.2% of the patients an equal or better result was seen one hour after administration of protocol A when compared to B1 and B2 respectively. In group B1 the percentage of the patients on which the administration of protocol A had an equal or lower effect decreased to 40.0% 2 hours after administration but rose again to 90.0% when assessed 4 hours after administration. In the same group

protocol A had a worse effect on the level of concentration in one patient 24 hours after administration in comparison to protocol B1 while it had a better effect in one patient of group B2 at the same point in time in comparison to protocol B2 (Figures 7g and 8g).

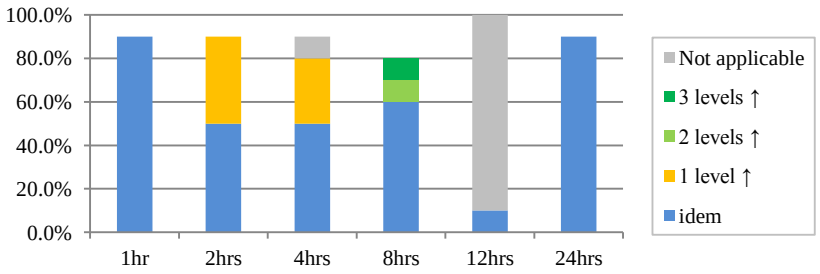
In none of the groups a negative effect was seen on the pattern of epileptic insults after administration of protocol A when compared to protocol B1 or B2. In one patient of group B1 a better effect was noticed when compared to protocol B1 (Figures 7h and 8h).

In group B1 a negative impact was reported on the sleeping pattern of 1 patient when protocol A was compared to protocol B1 (Figure 7i). In group B2 only an equal or better effect was seen when compared to protocol B2 (Figure 8i).

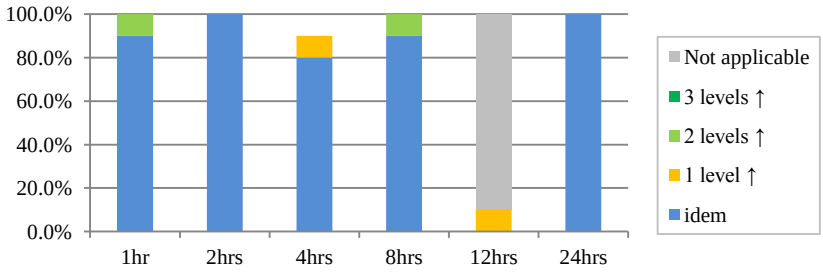
The results that focus on mood changes show that the impact of protocol A was equal or less in 50.0% of the patients of group B1 one hour after administration. In group B2 this percentage was 69.2%. Two hours after administration the percentage of patients with comparable or lower impact on mood changes was 70.0% and 69.2% when compared to protocol B1 and B2 respectively. Four hours and 8 hours after administration of protocol A these percentages rose to values between 69.2% and 80.0% in group B1 and B2. In both groups the impact 24 hours after administration of protocol A was less in one patient in comparison with the other protocols, while the effect was unfavourable in another patient. In all other cases the effect of protocol A was equal to the effect of the other protocols (Figures 7j and 8j).

Figure 9 shows the percentage of patients who got a negative score of their caregivers regarding their comfort level and behaviour, i.e. less favourable than their behaviour in normal circumstances. The results show that not all aspects were equally affected. When an impact was seen, this was most pronounced in the first 8 hours. The impact of protocol A dissipates faster than that of protocol B2, protocol B1 has the most long lasting impact. Focusing on the aspects of comfort and behaviour on which none of the patients received a negative score 1 hour after administration of protocols B1 or B2, the results show that after administration of protocol A also none of the patients received a negative score at the same point in time.

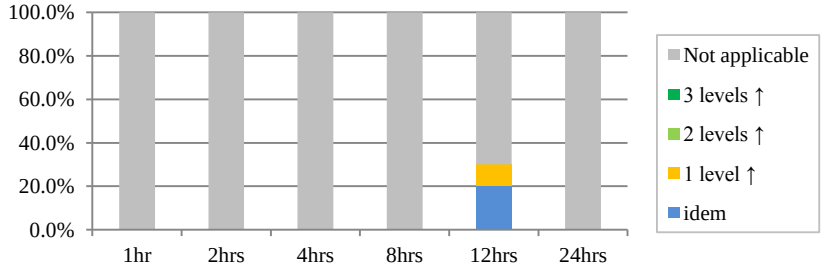
a. Appetite



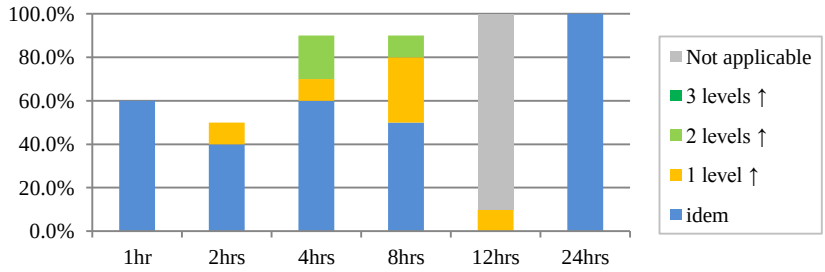
b. Toilet behaviour during the day



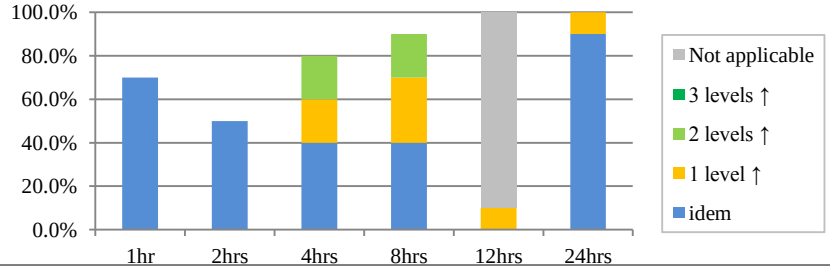
c. Toilet behaviour during the night



d. Fine motor skills



e. Gross motor skills



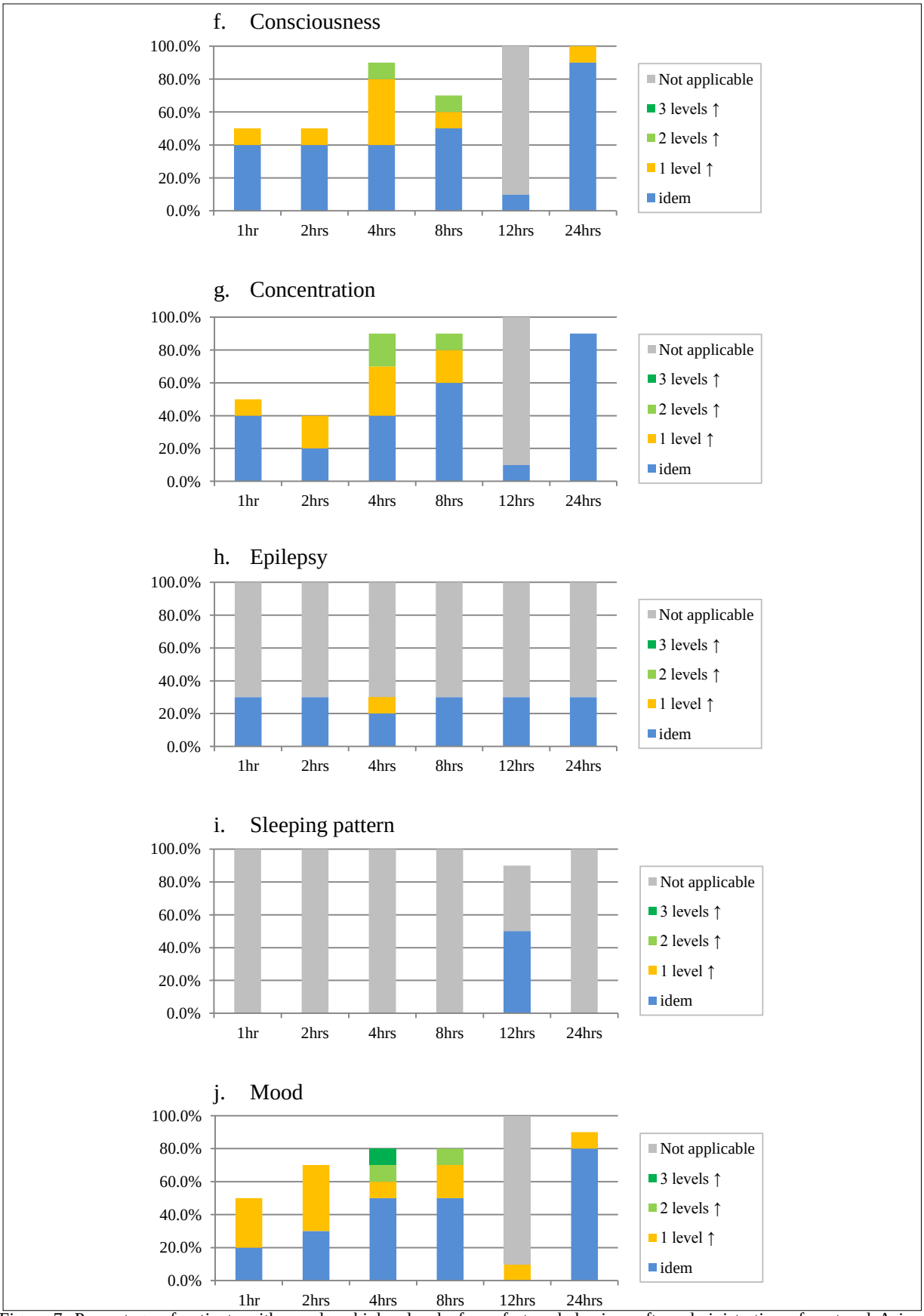
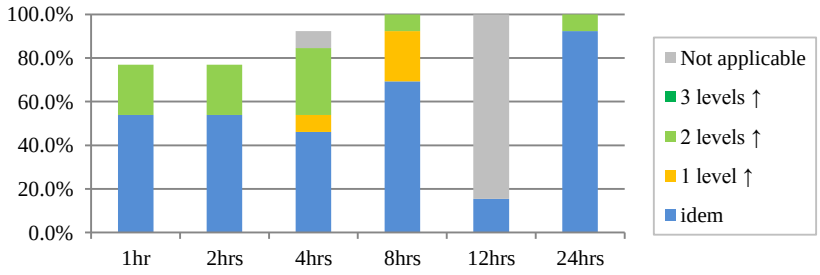
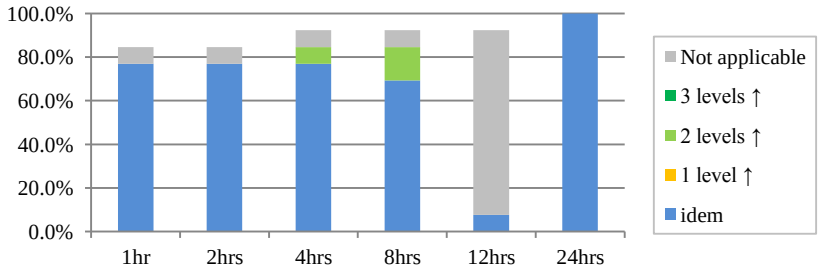


Figure 7: Percentage of patients with equal or higher level of comfort or behaviour after administration of protocol A in comparison to protocol B1 at different points in time (1, 2, 4, 6, 12 and 24 hours after administration of the sedative). Note that missing parts of the bars indicate patients with loss of comfort or negative impact on behaviour.

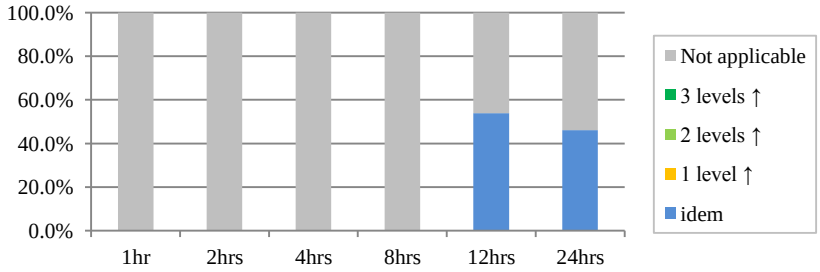
a. Appetite



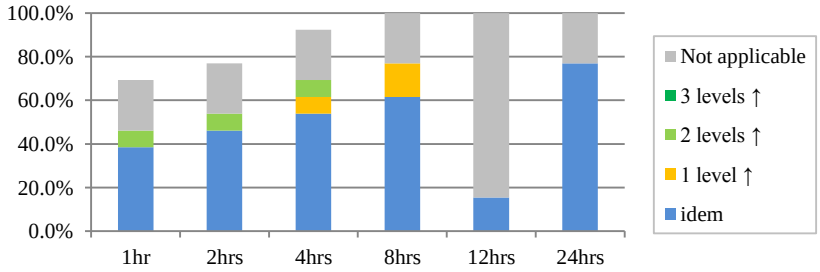
b. Toilet behaviour during the day



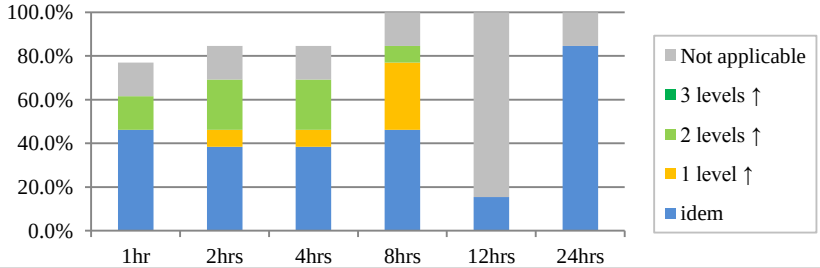
c. Toilet behaviour during the night



d. Fine motor skills



e. Gross motor skills



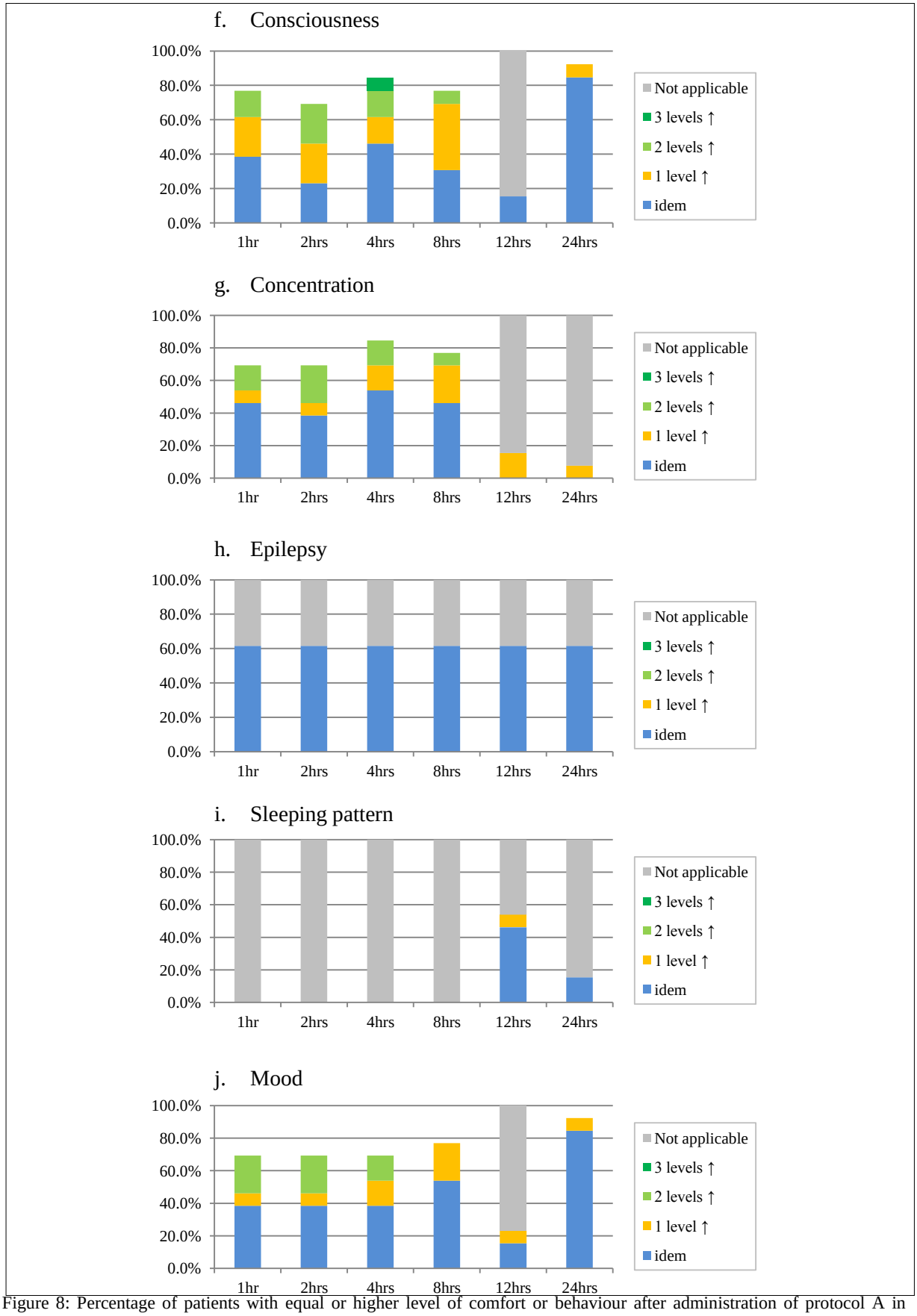


Figure 8: Percentage of patients with equal or higher level of comfort or behaviour after administration of protocol A in comparison to protocol B2 at different points in time (1, 2, 4, 6, 12 and 24 hours after administration of the sedative). Note that missing parts of the bars indicate patients with loss of comfort or negative impact on behaviour.

Figure 9: Percentage of patients who got a negative score of their caregivers regarding their comfort or behaviour at different points in time

Patient safety

Patient safety was evaluated by monitoring of vital parameters and consisted of measurements of blood pressure, pulse rate and oxygen saturation. Recordings were started before dental treatment and continued throughout dental treatment delivery, whenever the patient allowed this. No adverse reactions were recorded at any point in time, regardless which procedural sedation protocol was administered to the patient.

Discussion

Research presented in this paper aims to compare different procedural sedation protocols when applied in adults with a mental disability for the delivery of routine dental care.

Results show that, considering the evaluation by the dentist, the dental nurse and the patient's supervisors, the use of midazolam had at least the same effect on the level of cooperation during dental treatment in 90.0% of patients previously receiving lorazepam (B1) and 52.6% of patients receiving a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2). The effect was better in 66.7% of the patients receiving lorazepam (B1) and 28.9% of patients receiving a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2). This shows that midazolam is a good alternative for improving cooperation, mainly in patients previously receiving lorazepam. It should be emphasized however that even with more positive outcomes not all patients could be sedated at a level allowing dental treatment.

The differences in scores attributed by the different evaluators can possibly be explained by the fact that both the dental nurse and the supervisors of the patients know the patients in daily life. In contrast to the dentist, they know the patients when they are not sedated. This could have influenced their scoring behaviour during each of the dental treatment sessions in a positive or negative way. In addition, the nurse had knowledge of the patient's cooperation during previous dental treatment, since she has been working in the dental cabinet of the nursing home for many years. The dentist started working in the nursing home only recently, and therefore does not have this knowledge. For these reasons, the scores attributed by the dentist probably can be regarded as more objective. Further analyses, including larger groups of patients, are necessary to determine whether there is a significant difference in the scoring by the dentist, the dental nurse and the supervisors.

For none of the procedural sedation protocols an effect of gender of the patient on the level of cooperation was detected. A possible effect of body weight was not explored in the interim analyses presented here. However, both these items could be explored in a larger study sample.

In order to exclude a possible effect of the sequence of administration of the different procedural sedation protocols, this information was further analyzed. When comparing to the use of lorazepam (B1), there were no differences. However, when compared to the combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2) the sequence tended to have an influence with better outcomes for midazolam when used after using the combination of drugs. Further analysis using larger patient groups is necessary to provide an answer regarding statistical relevance.

Scales for the evaluation of the level of cooperation of adults with mental disability during dental treatment are hard to find. The most applicable for the purpose of this study was the scale of treatability as described by Van Grunsven[12]. However, even this scale was not fully adapted to the fact that the patients in this study were sedated, what made it nearly impossible to get the highest score.

A second and important part of the research considered the level of comfort for the patient.

The level of comfort and possible undesired behaviour after the sedation protocol were scored during 24 hours by the caregivers of the living group of the patients. Caregivers are in a perfect position for comparing these parameters in a situation without or with sedation. For most of the aspects of comfort and behaviour after sedation the majority of the patients received an equal or better score, when applicable, after administration of midazolam when compared to lorazepam (B1) or a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2) and this at all points in time. The caregivers of one patient who showed worse results on several aspects of comfort and behaviour and this at several time points after administration of midazolam, declared that this patient was generally ill at the day of dental treatment, possibly explaining the results.

When evaluating comfort and behaviour, caregivers were asked to define the exact number of levels of change ranging from much worse to much better. However, in the present report the overall effect (comparable, better or worse) was estimated to be more important than the exact number of levels of change. The latter can be investigated in further detail in a larger study sample.

Overall, midazolam had a shorter (negative) impact on comfort and behavior. The difference was most evident when compared to protocol B2.

Despite the fact that the results indicate that in the majority of the patients midazolam had a similar or better effect on the level of cooperation when compared to lorazepam (B1) or a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2), still there were patients who were scored as untreatable or uncooperative. However, there are arguments that advocate the replacement of lorazepam (B1) or a combination of diazepam, akineton, dehydrobenzperidol and atropine sulfate (B2) by the use of midazolam even in these cases. The most important reason is the fact that the results are indicative of increased comfort after the procedure.

In addition to the various aspects of comfort that were evaluated during this study, the route of administration is also an important advantage of midazolam. It can be assumed that drinking a little bit of apple juice is a more comfortable and enjoyable experience than an intramuscular injection as it is the case when using protocol B2.

Further, it should also be mentioned that a standard dose of 15 mg midazolam was used in all of the participants. An adjustment of this dose for those patients in which 15 mg was not enough to improve the cooperation to an acceptable level is a recommended topic for further research. In those patients where adjustment of the dose would not give the desired results, it should be kept in mind that perhaps deeper sedation or general anesthesia are better options[14].

In this study the dental treatment delivered consisted at each treatment session of a complete oral investigation and dental prophylaxis using an ultrasonic cleaning device. It might be speculated that results could have been different if local anesthesia, restorative procedures or surgical interventions would have been performed. This also is subject for further research.

The goal of using procedural sedation and the search for the best protocol is to perform the planned treatment in the most comfortable way for the patient. For those patients who could not be sedated using either of the protocols at a level allowing dental treatment, the exclusion of eventual oral causes of pain and discomfort was already a success. When treatment under deep sedation or general anesthesia was necessary, a more reliable preoperative treatment plan could be established.

It is fair also to mention the shortcomings of the research presented in this paper. The small number of participants and the fact that only an interim analysis was performed, lead to the fact that the results remain inconclusive. Further patient recruitment and statistical analysis is necessary.

Also, it was not possible to organize the dental treatment sessions in such a way that the patient was accompanied during both treatment sessions by the same supervisor. This is a variable with a possible impact on the assessment of the level of cooperation of the patient that could not be excluded. This may have introduced some bias.

Finally, it was assumed that all caregivers filled in the questionnaire as accurate as possible but it should be noted that they were not trained for this task and no calibration was organized before start of the study. Also this aspect may have introduced bias.

Conclusions

Preliminary results remain inconclusive but are indicative of increased comfort for the patient after dental treatment supported by midazolam when compared to each of the existing protocols used in this setting, while the level of cooperation when using this protocol was the same or even better in the majority of the patients according to the dentist, the dental nurse and the supervisor of the patient.
Patient recruitment will be continued. Final analysis of the results will determine whether the new protocol using midazolam will be adopted in nursing home Het Gielsbos.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgements

The authors would like to acknowledge the willingness and assistance of the managing board, the doctors, the nursing staff, the social workers, the caregivers, the parents who gave their permission and the residents of the nursing home Het Gielsbos during the study. We also thank Kathy Declerck for the management of the data.

References

1. Lewis C, Robertson AS, Phelps S. Unmet dental care needs among children with special health care needs: implications for the medical home. *Pediatrics*; 2005; 116: e426-e431.
2. Bottenberg P, Carvalho J, Declerck D, Declerck K, De Vos E, Vanden Abbeele A et al. Data registration and evaluation of the oral health of the Belgian population 2008-2010, final report. 2011.
3. Leroy R, Declerck D. Objective and subjective oral health care needs among adults with various disabilities. *Clin Oral Invest*; 2013; 17: 1869-1878.
4. Anders PL, Davis EL. Oral health of patients with intellectual disabilities: a systematic review. *Spec Care Dentist*; 2010; 30: 110-117.
5. Martens L, Marks L, Cauwels R. Verstandelijke beperkingen. In: De Mond, spiegel van gezondheid. Bijzondere aandachtsgroepen. Ed Martens L, Declerck D, Leroy R, Vanobbergen J, Acco Leuven/Den Haag; 2009; p. 386-389.
6. Dougall A, Fiske J. Access to special care dentistry, part 1. *Access Br Dent J*; 2008; 204: 605-616.
7. Nederlandse Vereniging voor Verstandelijke Gehandicapten. Richtlijnen voor farmacologische sedatie bij mensen met een verstandelijke handicap, 2001.
8. http://bijsluiters.fagg-afmps.be. Datum raadpleging 04/09/2013.
9. Heijnbrok – Van Herpen T, Bosma L, Vogel D. Handboek Enteralia: het toedienen van orale geneesmiddelen aan patiënten met een sonde of slikklachten. Springer, 2006. 127blz, p96.
10. Royal College of Paediatrics and Child Health. Medicines for children. 2003, 779blz, p412-413.
11. Medicatieklapper Kinderziekenhuis UZ-Leuven (intranet). Datum raadpleging 11/09/2013.
12. van Grunsven MF. Tandheelkundige zorg voor dieper-zwakzinnigen. Stafleu&Tholen B.V. Leiden, 1977 ISBN 90 6065 421 8
13. Leroy P. Improving procedural sedation in children. Doctoral Thesis, Maastricht 2012, 255blz, p155-196.
14. Glassman P. A review of guidelines for sedation, anesthesia, and alternative interventions for people with special needs. *Spec Care Dentist*; 2009; 29(1): 9-16.

Summary

Objectives To compare sedation protocols for dental care delivery in persons with mental disability.
Materials and methods Double-blind, cross-over clinical trial including mentally disabled residents (≥18 yrs, needing pharmacological support for dental care) of a nursing home. Procedural sedation using oral midazolam (15mg) (A) was compared to established protocols (already used in these patients): lorazepam (B1) or a combination of diazepam, biperideen, dehydrobenzperidol and atropine sulfate (B2). The test sequence was determined using randomization tables. Patient's level of cooperation during dental prophylaxis was scored independently (Van Grunsven scale) by the dentist, dental nurse and patient supervisor. Comfort level and side-effects afterwards were recorded by nursing staff (up to 24h after administration of the sedative). The study received ethical approval; informed consent was obtained from guardians.
Results 23 patients (10 in group B1, 13 in group B2) were enrolled (12 male, 11 female; 16-59 yrs). According to the dentist cooperation when using protocol A was at least equal in 80.0% and even better in 60.0% of the cases when compared to protocol B1. The dentist evaluated the cooperation when using protocol A at least equally in 61.5% of the cases and even better in 30.8% when compared to protocol B2. For most of the aspects of comfort and behaviour afterwards the majority of the patients got an equal or better score, when applicable, after administration of protocol A when compared to protocol B1 or B2 for all points in time.
Conclusions Preliminary results remain inconclusive but are indicative of increased comfort after the procedure when using midazolam while the level of cooperation when using this protocol was the same or even better in the majority of the patients during regular dental treatment. Patient recruitment will be continued, allowing advanced statistical analyses.
Clinical Relevance This study aims to assess whether the adoption of a new protocol presents an improvement for patient care, i.e. allows regular dental care to be performed under at least the same conditions as with the currently used protocol but with less discomfort for the patients (shorter effect) and without additional side-effects. This research will therefore contribute to the optimization of dental care in this specific population.

Keywords Mental disability; Dental care; Procedural sedation; Adults; Midazolam

Critical Reflection

Het Gielsbos is a nursing home for people with a mental disability. About 20 years ago a dental cabinet was installed to provide regular dental care to all residents. Since two years I am the dentist of this facility. Here I have got my first experience with procedural sedation, which has been used in the facility for many years.

In my job as dentist for patients with a mental disability it is my priority to make dental treatment as comfortable as possible. That is why I wanted to become more familiar with the technique and started to search for more information in the literature, but instead more questions arose. There is so little research available about procedural sedation in this particular population and I didn't understand why. However, what I did find was that the protocol used in the nursing home presented considerable risks for adverse events. At the same time I got remarks of the caregivers of the nursing home that some of the residents were burdened by the sedation even long after the dental treatment.

When looking for alternative solutions I realized that I could not find any suitable protocol to solve this issue. At that moment the idea rose to do some research on my own. This was easier said than done. I experienced a lot of obstacles in my way while I was trying to start my research project.

First I tried to find an alternative protocol in the literature to compare with the current one. After a couple of months I still had not found one. Thanks to professor Declerck I got the opportunity to meet Mrs. Elinor Bouvy. She has a lot of experience in The Netherlands with procedural sedation for dental treatment in people with a mental disability and she taught me their protocol as used in the Centre for Special Care Dentistry CBT Rijnmond. It is based on the guidelines of the Dutch Society for Mentally Disabled on pharmacological sedation for people with a mental disability of 2001.

The next challenge was to find a validated scale to evaluate the level of anxiety and cooperation of patients with a mental disability during regular dental treatment. There are many scales for adult patients, even a lot of modified scales for children, but it was very difficult to find one for this specific population. It was once again Mrs. Elinor Bouvy who suggested us to use the scale of Van Grunsven.

The main purpose of the research was selecting a protocol that potentially would improve the cooperation of the patients, but the comfort of the patients afterwards was at least as important. To evaluate this comfort of the patient afterwards, I designed a questionnaire that had to be filled in during 24 hours after dental treatment based on a questionnaire used by Mrs. Elinor Bouvy in previous studies.

After writing down the study protocol it was my job to convince the doctors and staff of the nursing home of the importance and necessity of this project. Of course they also want the best for the residents and the population of mentally disabled in general, but there were still some doubts about the new protocol. Thanks to the help of professor Declerck we succeeded to come to an agreement about the research project and the protocol under investigation.

The last thing to do, I thought, was to submit the protocol to the Clinical Trial Center for ethical approval, but the truth didn't meet my expectations at all. The Clinical Trial Centre stated that is was necessary to get the approval of the commission Medische Ethiek UZLeuven and the Federal Agency for Medicines and Health Products because of the fact that the research focuses on medicines. This was not easy at all. Our case was handled as if we had the intention to bring a new medicine on the market. As a consequence it took me 3 months to get the final approval.

But my patience paid off. After facing so many obstacles I now have got my answer why there is so little literature about research on procedural sedation during dental treatment in people with a mental disability. It is very easy to get discouraged along the way. I am very proud I can say that I held on and I finally can present the first results of the research project.

This experience makes that from now on I will read literature with another perspective.

Attachments

1. Protocol
2. Indeling van behandelbaarheid volgens Van Grunsven (1977)
3. 24-uursrapportage n.a.v. tandheelkundige behandeling met premedicatie. Registratie en evaluatie door begeleiding.
4. Informed consent

Attachment 1: Protocol

Optimization of procedural sedation protocol used for dental care delivery in people with mental disability

Protocol Acronym: OptiSeDent

Version 2: November 4, 2013

Trial identifiers

EudraCT Number: 2013-003991-11
NCT (clinicaltrials.gov): NCT02078336

Sponsor:

Name: Katholieke Universiteit Leuven (KU Leuven)
Address: Oude Markt 13, 3000 Leuven

Principal Investigator:

Name: Professor Dominique Declerck
Address: Kapucijnenvoer 7 blok a bus 7001, 3000 Leuven
Telephone: +32 16 332307
Fax: +32 16 332752
Email: Dominique.declerck@med.kuleuven.be

Sub-investigator:

Name: Ine Opsomer
Address: Kapucijnenvoer 7 blok a bus 7001, 3000 Leuven
Email: ine.opsomer@uzleuven.be

Signatures

_____ _____

Principal Investigator Date

Print Name: Dominique DECLERCK

_____ _____

Date

Print Name: Ine OPSOMER

Table of Contents

1. Study Synopsis

Title of clinical trial	Optimization of procedural sedation protocol used for dental care delivery in people with mental disability
Study Phase if not mentioned in title	Phase IV
Sponsor name	Katholieke Universiteit Leuven
Principal Investigator	Professor Dominique Declerck
EudraCT number	2013-003991-11
Medical condition or disease under investigation	Limited cooperation of people with mental disability during regular dental care delivery
Purpose of clinical trial	Comparison of procedural sedation protocols used for dental care delivery in patients with mental disability
Primary objectives	To assess the **level of cooperation** during regular dental care using different procedural sedation protocols To assess **patient safety** during regular dental care using different sedation protocols To assess **patient comfort and possible side-effects** after regular dental care using different sedation protocols
Secondary objective (s)	-

Trial Design	Randomized Clinical Trial Double Blind-Cross Over design
Endpoints	- Level of cooperation during regular dental care delivery - Recording of blood pressure, pulse, oxygen saturation during regular dental care delivery - Level of patient comfort and possible side-effects after dental treatment session, including: - changes in appetite - changes in toilet behaviour - changes in level of consciousness - changes in level of concentration - changes in pattern of epileptic insults - changes in mood - changes in sleeping pattern - changes in level of motor skills
Sample Size	40 patients, in 2 groups: - 20 patients protocol A vs protocol B1 - 20 patients protocol A vs protocol B2
Summary of eligibility criteria	- Minimum age 18yrs - Patient resides at least 6 months in nursing home “het Gielsbos”. - Patient always gets a sedative protocol to make dental care delivery possible. - Informed consent was obtained from parent/guardian - No medical contra-indication for any of tested sedative protocols
IMP, dosage and route of administration	Midazolam, dose of 15mg, oral administration (referred to as ‘**Protocol A**’)

Active comparator product(s)	**Protocol B1**: Lorazepam, dose of 2.5mg, oral administration **Protocol B2:** Cocktail with following composition: - Diazepam, dose of 10mg, IM - Biperideen, dose of 5mg,IM - Dehydrobenzperidol, dose of 3.125mg/m^2 body surface, IM - Atropine sulfate, dose of 0,25mg, IM
Maximum duration of treatment of a Subject	Each subject will receive two (scheduled) dental treatment sessions (each of approximately 30 minutes duration) with alternating (random order) administration of test protocol and standard sedation protocol; with 24 hours follow-up after the procedure.
Version and date of final protocol	Version 2, November 4, 2013

2. Background and rationale

Delivery of dental care in people with a mental disability is very demanding and presents many challenges. Among these are the limitations of the patient to cope with the dental treatment. This necessitates in many cases treatment provision under general anesthesia, requiring treatment delivery in a hospital setting. As a consequence, small dental interventions and regular preventive treatments are often postponed with negative impact on the quality of life and long-term (oral) health of the individual as a result.

An alternative is the use of procedural sedation. This technique has been widely used in 'Het Gielsbos', a nursing home for people with a mental disability. For many years already, patients in need of medicinal support for dental care delivery receive lorazepam or a cocktail based on diazepam. In recent scientific literature however, midazolam is the sedative of first choice for procedural sedation[1]. Main reasons for this are: rapid absorption of the drug, rapid transportation, rapid metabolization and short half-life.

It is important that the procedural sedation of people with mental disability when receiving dental care can be applied in a safe way, based on sound indications and with high effectivity. This study aims to assess whether the adoption of a new protocol presents an improvement for patient care, i.e. allows regular dental care to be performed under at least the same conditions as with the currently used protocol but with less discomfort for the patients (shorter effect) and without additional side-effects. This research will therefore contribute to the optimization of dental care in this specific population.

3. Trial objectives and Design

3.1 Trial objectives

The study aims to compare the proposed procedural sedation protocol with currently used sedation protocols, specifically applied for the delivery of regular dental care in persons with a mental disability.

The objectives are:

- to assess the **level of cooperation** during regular dental care using different sedation protocols
- to assess **patient safety** during regular dental care using different sedation protocols
- to assess **patient comfort and possible side-effects** after regular dental care using different sedation protocols

3.2 Primary endpoints

The primary endpoints of the study are:

- level of cooperation of patient when receiving regular dental care

This endpoint will be assessed using the scale published by Van Grunsven[2].

3.3 Secondary endpoints

- Recording of blood pressure, pulse, oxygen saturation during regular dental care delivery
- Level of patient comfort and possible side-effects after dental treatment session, including:
    - changes in appetite
    - changes in toilet behaviour
    - changes in level of consciousness
    - changes in level of concentration
    - changes in pattern of epileptic insults
    - changes in mood
    - changes in sleeping pattern
    - changes in level of motor skills

This endpoints will be assessed using a questionnaire[3].

3.4 Trial Design

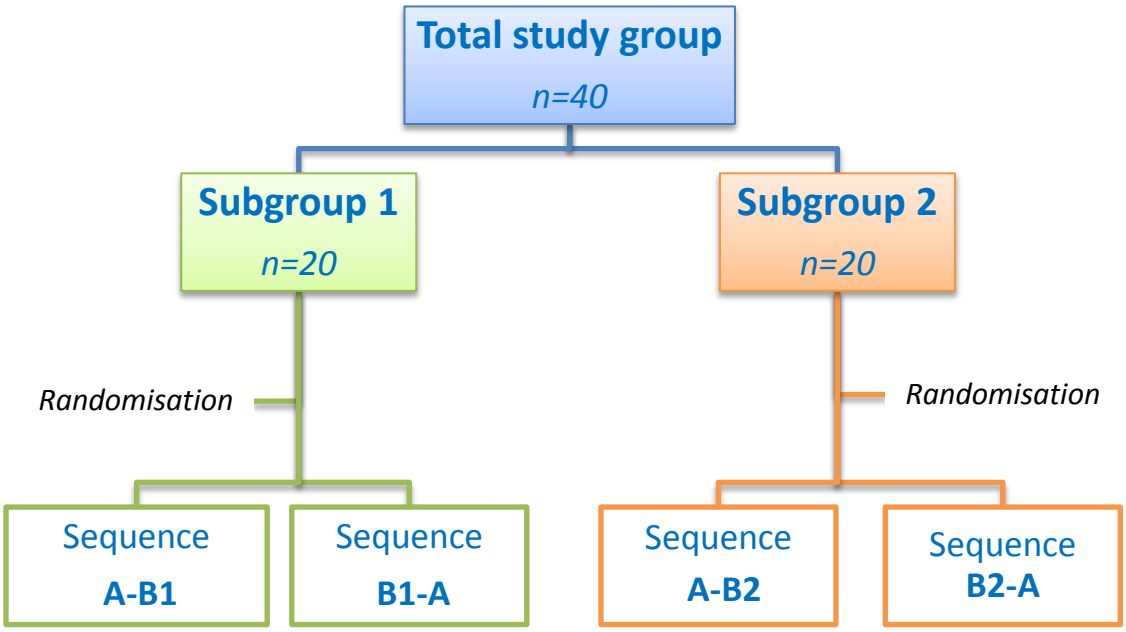
This trial will include two groups (patients receiving either protocol B1 or B2 as standard sedative protocol (since many years) when receiving dental care) and will be conducted with randomization of subjects within those two groups in again two groups, using a cross-over design and with double blinding (patients/caregivers and operator (dentist)).

3.5 Study diagram

The study will be performed according to the schematic representation below.

Patients eligible for participation to the study will be included in Subgroup 1 or 2, based on the sedative protocol they are receiving for dental care delivery before entering the study. Below both these protocols are detailed and referred to as B1 or B2. Patients will be included until the number of 20 patients per subgroup is reached.

Within both subgroups, a randomization scheme will be used to determine the sequence of treatment allocation (alternated administration of the 'new' sedation protocol (referred to as A) and the subject's standard sedation protocol (B1 or B2)).



3.6 Trial Flowchart

	Before 1st dental treatment session	1st dental treatment session	0-24h after 1st dental treatment session	Before 2nd dental treatment session	2nd dental treatment session	0-24h after 2nd dental treatment session
Informed consent	X					
Physical examination	X			X		
Administration of sedative (A or B1/B2)	X			X		
Scoring[2] cooperation during dental treatment		X			X	
Monitoring of vital parameters[13]		X			X	
Scoring[3] comfort of the patient after dental treatment			X			X

4. Trial Medication

4.1 Investigational Medicinal product and dosing regimen

The sedative will be administered by the nurse of the facility in the presence of a physician between 45 minutes and 1 hour before the start of the scheduled dental treatment.

Protocol A

- Midazolam Mylan[4] 5mg/ml
  - IV-ampules of 1ml, administered by oral route[10, 11, 12]
  - Dose of 15 mg, dissolved in apple juice[12]
  - Marketing Authorization holder:
    Mylan bvba/sprl
    Terhulpsesteenweg 6A
    B-1560 Hoeilaart
  - BE339385

Protocol B1

- Lorazepam Mylan[5] 2.5mg
  - Tablets for oral intake
  - Dose of 2.5mg (1 tablet)
  - Marketing Authorization holder:
    Mylan bvba/sprl
    Terhulpsesteenweg 6A
    B-1560 Hoeilaart
  - BE193681

Protocol B2:

Cocktail based on:

- Valium[6] 10mg/2ml
  - Solution for injection
  - Dose: 10mg
  - Marketing Authorization holder
    N.V. Roche S.A.
    Dantestraat 75
    B-1070 Brussel
  - BE054871
- Akineton[7] 5mg/1ml
  - Solution for injection
  - Dose: 5mg

    - Marketing Authorization holder
      Laboratorio Farmaceutica
      Via Cavour 70
      27035 Mede (PV)
      Italië
    - RVG02197
- Dehydrobenzperidol[8] 5mg/2ml
    - Solution for injection
    - Dose: 3.125mg/m^2 body surface
    - Marketing Authorization holder:
      ProStrakan Ltd.
      Galabank Business Park
      Galashiels
      TD1 1QH
      Verenigd-Koningrijk
    - BE098777
- Atropine sulfate Sterop[9] 0.25mg/1ml
    - Solution for injection
    - Dose: 0.25mg
    - Marketing Authorization holder:
      Laboratoria STEROP n.v.
      Scheutlaan 46-50
      1070 Brussel
    - BE344635

4.2 Drug accountability

Sedative drugs will be administered by the nurse responsible for the study participant; in case of impossibility to administer the drug the nurse will mention this in the patient file.

4.3 Subject compliance

A nurse of the nursing home will administer the medication to the patients. In case of oral administration, she will make sure that the medication is completely swallowed by the patient.

4.4 Concomitant medication (non-IMP)

Standard medications or treatments will be continued concurrently with the study medication. In case of changes to the standard medication of the patient, this will be mentioned explicitly in the patient file. Rescue medication (with purpose “relief of symptoms”) is not applicable in this study.

5. Selection and withdrawal of subjects

5.1 Inclusion criteria

Inclusion criteria are the following:

- Minimum age of 18yrs

- The patient resides at least 6 months in nursing home “het Gielsbos”.

- The patient always gets medicinal support to make dental care possible.

- Informed consent is obtained from a parent or the guardian of the patient.

- No medical contra-indication for any of the sedative protocols

5.2 Exclusion criteria

Exclusion criteria are the following:

- Age under 18yrs

- The patient is no resident of the nursing home “het Gielsbos” or lives there for less than 6 months.

- No need for medicinal support during dental treatment

- No informed consent was obtained by parents or the guardian of the patient.

- Medical contra-indication for 1 of the sedative protocols, for example there will be no administration of dehydrobenzperidol to people with prolonged QT-interval.

5.3 Selection of participants

The participants will be recruited among residents of the nursing home “Het Gielsbos”.

5.4 Randomization procedure/Code Break

The physician attached to the nursing home will use a randomization table to determine the sequence in which the sedation protocol will be administered. The physician and nurse, who administer the medicine, are the only persons that know which sedation protocol was applied at the moment of dental care delivery. They are not involved in the evaluation of the primary objectives. The sequence is entered in the data file after the last patient received his second treatment session and was followed-up for at least 24 hours.

5.5 Withdrawal of subjects

Subjects (or their guardian) can decide to withdraw from the study at any moment (part of informed consent).
In case of relevant changes in the medical condition of the patient, the physician of the nursing home can decide to withdraw the subject from the study.

5.6 Expected duration of trial

The period between first patient treatment session and last patient treatment session (including follow-up period) is estimated to be about 9 months.

6. Trial Procedures

6.1 By visit

1. The physician of the nursing home “Het Gielsbos” will perform a physical examination of the subject in order to determine whether the patient can be administered both of the investigated sedative protocols.

2. The physician determines the sequence of administration of both protocols using a randomization table with sequences A-B1/B2 or B1/B2-A.

3. The patient receives the sedative between 45 minutes and 1 hour before the start of the scheduled dental treatment. The sedative is administered by the nurse.

4. The patient receives scheduled regular dental care. Monitoring of vital parameters starts before starting the dental treatment and continues throughout dental treatment delivery.
During and after dental treatment the dentist, the dental assistant and the supervisor of the patient will independently score the level of cooperation of the patient using the scale described by Van Grunsven[2].

5. After dental treatment, the caregivers of the nursing home will score the comfort of the patient and any possible side-effects during 24 hours using a questionnaire[3].

6.2 Laboratory tests

No laboratory tests planned.

6.3 Other investigations

No other investigations planned.

7. Assessment of efficacy

During and after dental treatment the dentist, the dental assistant and the supervisor of the patient will independently score the level of cooperation of the patient using the scale described by Van Grunsven[2].

8. Assessment of Safety

8.1 Specification, timing and recording of safety parameters[13]

- Before any of the proposed sedative protocols is administered, the physician performs a physical examination.
- The medication is administered in the presence of a physician.
- During dental treatment, vital parameters are continuously measured with the aid of a pulse oximeter.
- The dentist performing dental treatment is trained in Basic Life Support and is capable of recognizing respiratory insufficiency and circulatory threatening states.
- Every dental treatment session performed with medicinal support will be recorded in detail in the patient file.
- The patient will be carefully observed during 24h after the dental treatment.
- An antagonist, flumazenil, is available.
- All adverse events will be reported as mentioned under 8.2.

8.2 Procedures for recording and reporting adverse events (AE)

8.2.1 Definitions in Law of May 7, 2004 concerning experiments on the human person

Adverse reaction (AR): all untoward and unintended responses to an investigational medicinal product or to an experiment and, when an investigational product is concerned, related to any dose administered;

Adverse event (AE): any untoward medical occurrence in a patient or subject of the treated group during an experiment, and which does not necessarily have a causal relationship with this treatment;

Unexpected adverse reaction (UAR): an adverse reaction, the nature or severity of which is not consistent with the information on the experiment, and, when a clinical trial is concerned, with the applicable product information (e.g. investigator's brochure for an unauthorized investigational product or the patient leaflet joined to the summary of product characteristics for an authorized product);

Serious adverse event (SAE) or serious adverse reaction (SAR): any untoward medical occurrence or effect that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect, and this, when it is a clinical trial, at any dose;

Suspected unexpected serious adverse reaction (SUSAR): is an AR that isserious and unexpected (meaning that nature or severity of the AR is not consistent with the Investigational Medicinal Product reference safety information, which is the Investigator's Brochure) and is judged by either the investigator or the sponsor as having a reasonable suspected causal relationship with the investigational medicinal product.

8.2.2 Notification of adverse events

The investigator shall report all serious adverse events immediately, after first knowledge, to the sponsor except for those that the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate report shall be followed by detailed, written reports. The immediate and follow-up reports shall identify subjects by code numbers.

The sponsor shall keep detailed records of all adverse events which are reported to him by the investigator or investigators. These records shall be submitted to the competent Belgian authorities.

8.2.3 Notification of serious adverse reactions

The sponsor shall ensure that all relevant information about suspected unexpected serious adverse reactions that are fatal or life-threatening is recorded and reported as soon as possible to the competent Belgian authorities, and to the competent ethics committee, and in any case no later than seven days after knowledge by the sponsor of such a case, and that relevant follow-up information is subsequently communicated within an additional eight days.

All other suspected unexpected serious adverse reactions shall be reported to the competent Belgian authorities and to the ethics committee concerned as soon as possible but within a maximum of fifteen days of first knowledge by the sponsor.

Regarding those adverse events and serious adverse reactions the Principal Investigator will take all reasonable measures, in consultation with Sponsor, to protect subjects at risk following the occurrence of such events.

8.2.4 Adverse events that do not require reporting

Since medications administered within this trial are licensed, events or reactions listed in the SmPC[4,5,6,7,8,9] do not need to be reported. The period for AE reporting is 24 hours post final IMP administration.

8.3 Treatment stopping rules

No rules defined.

8.4 Data monitoring committee (DMC)

No data monitoring committee established.

9. Statistics

9.1 Sample size

In order to be able to detect a 20% difference in level of patient cooperation with a confidence level set at 5%, it was calculated that 20 patients needed to be included in each subgroup, leading to a total of 40 study patients.

9.2 Randomization

The application of a randomization protocol with cross-over design should minimize bias.

For randomization purposes, a computer generated sequence table will be produced. The only persons having knowledge of the sequence of drug administration (at moment of dental treatment) are the physician and nurse of the nursing home.

9.3 Analysis

Statistical analysis will include all patients having received both sedative protocols. In case of incomplete data, a detailed analysis of reasons for missingness of data will be performed.

Interim analyses are not planned.

The data will be statistically processed with the aid of a paired analysis with a significance level set at 0.05.

10. Quality assurance

Quality assurance measures include:

- strict definition of inclusion and exclusion criteria
- written protocol for administration of sedative protocols
- supervised administration of medication
- use of standardized scoring method for measuring level of cooperation
- detailed instructions to dental assistant for recording of level of cooperation
- use of standardized scoring forms for assessing comfort of patients and possible side effects

11. Direct access to source data and documents

Investigator(s) and the institution will permit trial-related monitoring, audits, EC review, and regulatory inspections (where appropriate) by providing direct access to source data and other documents (i.e. patients' case sheets, scoring forms etc).

12. Ethics and regulatory approvals

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (2008), the principles of GCP and in accordance with all applicable regulatory requirements. This protocol and related documents will be submitted for review to the relevant Ethics Committee and to the Federal Agency for medicinal products for Clinical Trial Authorization.

Ethics Committee:
Commissie Medische Ethiek van Universitaire Ziekenhuizen KU Leuven
Campus Gasthuisberg
Herestraat 49
B-3000 Leuven

The Study can and will be conducted only on the basis of prior informed consent by the Subjects, or their legal representatives, to participate in the Study. The Participating Site shall obtain a signed informed consent form (ICF) for all patients prior to their enrollment and participation in the Study in compliance with all applicable laws, regulations and the approval of the (local) Ethics Committee, if required. The Participating Site shall retain such ICFs in accordance with the requirements of all applicable regulatory agencies and laws.

Any subsequent protocol amendments will be submitted to the EC and Regulatory Authorities for approval.

The Investigator and the Participating Site shall treat all information and data relating to the Study disclosed to Participating Site and/or Investigator in this Study as confidential and shall not disclose such information to any third parties or use such information for any purpose other than the performance of the Study. All the data are coded. The collection, processing and disclosure of personal data, such as patient health and medical information are subject to compliance with applicable personal data protection and the processing of personal data (Directive 95/46/EC and Belgian law of December 8, 1992 on the Protection of the Privacy in relation to the Processing of Personal Data).

13. Data Handling

During and after dental treatment the dentist, the dental assistant and the supervisor of the patient will independently score the level of cooperation of the patient using the scale described by Van Grunsven[2]. This data will be collected immediately by the dentist herself.

After dental treatment, the nursing staff of the nursing home will score the comfort of the patient during 24 hours using a questionnaire[3]. This data will be collected by the nursing staff and handed over to the dentist.

14. Data Management

Data will be entered in an electronic database using Excel Microsoft (Office 2007) and exported to SAS for statistical processing.

15. Translational research

There will be no collection of biological material.

16. Publication Policy

The results of this study will be part of a master thesis at the KU Leuven (Master in Specialistische Mondgezondheidszorg, optie Kindertandheelkunde & Bijzondere zorgverlening) and will be presented to the staff and collaborators of the unit of Paediatric Dentistry and Special Care of the UZLeuven. The presentation of the results will be based on summary measures; individual data will never be presented. Publications will be coordinated by the Investigator or Sponsor. Authorship to publications will be determined in accordance with the requirements published by the International Committee of Medical Journal Editors and in accordance with the requirements of the respective medical journal.

17. Insurance/Indemnity

In accordance with the Belgian Law relating to experiments on human persons dated May 7, 2004, Sponsor shall assume, even without fault, the responsibility of any damages incurred by a Study Patient and linked directly or indirectly to the participation to the Study, and shall provide compensation therefore through its insurance.

18. References

1. Annex 1: Richtlijnen voor farmacologische sedatie bij mensen met een verstandelijke handicap 2001, Nederlandse Vereniging voor Verstandelijke Gehandicapten
2. Annex 2: Tandheelkundige zorg voor dieper-zwakzinnigen. MF van Grunsven. Stafleu&Tholen B.V. Leiden, 1977 ISBN 90 6065 421 8
3. Annex 3: 24-uursrapportage n.a.v. tandheelkundige behandeling met premedicatie. Registratie en evaluatie door begeleiding.
4. Annex 4: Samenvatting van de Productkenmerken: Midazolam Mylan 5 mg/ml oplossing voor injectie
5. Annex 5: Samenvatting van de Productkenmerken: Lorazepam Mylan 2,5 mg tabletten
6. Annex 6: Samenvatting van de Productkenmerken: Valium 10 mg/2ml oplossing voor injectie
7. Annex 7: Samenvatting van de Productkenmerken: Akineton 5mg/1ml oplossing voor injectie
8. Annex 8: Samenvatting van de Productkenmerken: Dehydrobenzperidol 5mg/2ml oplossing voor injectie
9. Annex 9: Samenvatting van de Productkenmerken: Atropine sulfate Sterop 0,25mg/1ml oplossing voor injectie
10. T. Heijnbrok – Van Herpen ea. Handboek Enteralia: het toedienen van orale geneesmiddelen aan patiënten met een sonde of slikklachten. Springer, 2006. 127blz., p96.
11. Royal College of Paediatrics and Child Health. Medicines for children. 2003, 779blz, p412-413.
12. Medicatieklapper Kinderziekenhuis UZ-Leuven (intranet). Datum raadpleging 11/09/2013.
13. P. Leroy. Improving procedural sedation in children. Doctoral Thesis, Maastricht 2012, 255blz, p155-196.

Attachment 2: Indeling van behandelbaarheid volgens Van Grunsven

INDELING VAN BEHANDELBAARHEID VOLGENS VAN GRUNSVEN

De indeling van Grunsven kan een leidraad om in de toekomst verder uit te werken aan de hand van de rapporten 'kwaliteitskader Gehandicaptenzorg', 'kwaliteitscriteria vrijheidsbeperking' en 'Goede zorg bij verzet'.

IV **Coöperatief**	– Goed contact met de tandarts, verbaal of door middel van gebaren; – Toont belangstelling voor wat er gebeurt; – Ligt ontspannen in de behandelstoel; – Werkt mee bij het onderzoek voor zover daartoe ook motorisch in staat;
III **Passief**	– Geen contact; – Ligt niet merkbaar gespannen in de behandelstoel; – Laat verschillende onderdelen van het onderzoek passief toe; – Moet bij alles geholpen worden, maar verzet zich daar niet tegen;
II **Weifelend**	– Erg behoedzaam; – Probeert met vertragingstechnieken het onderzoek uit te stellen; – Moet duidelijk wennen aan de situatie, maar pogingen om de behandeling te ontvluchten kunnen steeds weer gecorrigeerd worden;
I **Niet-Coöperatief**	– Geeft verbaal en/of fysiek duidelijk blijk van ongenoegen; – Moet in de behandelstoel worden vastgehouden; – Kalmeert na enige tijd, maar blijft het gehele onderzoek perioden van verzet tonen;
0 **Onbehandelbaar**	– Onafgebroken verzet, dat binnen een periode van 10 minuten niet te beïnvloeden is.

Attachment 3: 24-uursrapportage n.a.v. tandheelkundige behandeling met premedicatie. Registratie en evaluatie door begeleiding

Optimalisatie van medicamenteuze ondersteuning bij tandheelkundige zorgverlening aan personen met een verstandelijke beperking.

REGISTRATIE & EVALUATIEDOOR BEGELEIDING

Momenteel wordt er in het Gielsbos een **project** gevoerd met betrekking tot de **medicatie** die sommige bewoners krijgen vóór een **tandheelkundige behandeling**. De informatie verkregen via dit project moet het mogelijk maken zicht te krijgen op welke medicatie het meest effectief is tijdens tandheelkundige zorgverlening. Daarnaast moet het ook een idee geven van de nawerking van de medicatie nadat de bewoner het tandheelkundig kabinet heeft verlaten. Deze informatie is noodzakelijk bij de keuze van premedicatie voor tandheelkundige behandeling van de bewoners van het Gielsbos. Ook de ervaringen van de begeleiding/leefgroep vormen hier een belangrijk onderdeel van. Om dit in kaart te kunnen brengen, vragen we **uw medewerking** via het invullen van het bijgevoegd formulier. Indien iets onduidelijk is of wanneer er problemen zijn, kan u steeds terecht bij tandarts Ine Opsomer (ine.opsomer@hetgielsbos.be).

Mogen we u vragen om de volledig ingevulde lijst terug te bezorgen via de <u>VERPLEGING</u>

Lees dit vooraf:

- Afhankelijk van de vraag:
  - Kruis het vakje aan dat overeenkomt met het voor u meest passende antwoord
  - Vul het symbool in dat overeenkomt met uw antwoordkeuze
  - Vul aan met vrije tekst
- Helemaal achteraan de vragenlijst kan u nog aanvullende opmerkingen en suggesties noteren.

Wij danken u voor uw medewerking!

Naam bewoner: ……

Leefgroep: ……

Datum tandheelkundige behandeling: ……/……/2013

Beantwoord onderstaande vragen door in elk vakje het symbool te plaatsen dat het best overeenkomt met uw bevindingen. Er dient steeds een vergelijking gemaakt te worden met hoe de bewoner normaal gemiddeld functioneert.

Antwoordmogelijkheden:
(--) duidelijk negatief effect, duidelijk veel zwakker
(-) licht negatief effect, zwakker
(0) geen effect, zoals bewoner normaal functioneert
(+) licht positief effect, beter
(++) duidelijk positief effect, duidelijk veel beter

	….	….	….	….	….	….
Naam begeleider						
Is er een verandering in eetlust?						
Is er een verandering in toiletgedrag overdag?						
Is er een verandering in toiletgedrag ‘s nachts?						
Is er een effect op de fijne motoriek? (vb. knippen, schrijven, …)						
Is er een effect op de grove motoriek? (vb. lopen, zwemmen…)						
Is er een verandering in bewustzijn?						
Is er een verandering in concentratie?						
Is er een verandering in graad van epilepsie?						
Is er een verandering in nachtrust?						
Is er een verschil in gemoedstoestand?						

Uw mening

Noteer hieronder eigen opmerkingen, bedenkingen en suggesties:

Hartelijk dank voor uw medewerking!

Attachment 4: Informed consent

Beste ouder of voogd,

Aan de hand van deze informatiebrief willen wij u op de hoogte brengen van een project dat zal plaatsvinden in het Gielsbos en waarvoor wij u de mogelijkheid bieden tot deelname.

Voordat u beslist of u al dan niet zal deelnemen, is het belangrijk dat u de informatie volledig doorneemt zodat het voor u duidelijk is waarom dit project gepland wordt en wat deelname inhoudt.

Neem rustig de tijd om deze informatie door te nemen. Indien iets onduidelijk is of indien u nog bijkomende informatie wenst, kan u die bekomen via de contactpersonen vermeld onderaan deze informatiebrief.

"Optimalisatie van medicamenteuze ondersteuning bij tandheelkundige zorgverlening aan personen met een verstandelijke beperking"

Wat is het doel van dit project?

Voor het uitvoeren van tandheelkundige zorgen krijgen sommige personen met een mentale beperking vooraf medicatie toegediend om rustiger te worden en zo de verzorging mogelijk te maken. Zo kan op een veilige wijze kwaliteitsvolle zorg aangeboden worden aan deze personen.

In het Gielsbos wordt deze methode reeds vele jaren toegepast, volgens een vast protocol. Ervaringen uit andere centra en ook gegevens uit de literatuur geven aan dat er aangepaste protocols bestaan die met eenzelfde effect en vergelijkbare veiligheid kunnen toegepast worden. Een voordeel van deze aangepaste protocols is dat de nawerking na de behandeling minder groot is wat comfortabeler is voor de persoon en zijn begeleiders.

Doel van het project is om na te gaan of dit aangepast protocol comfortabeler wordt ervaren door de bewoners en/of begeleiding en tevens toelaat om tandheelkundige zorgen uit te voeren op een vergelijkbare manier als met het huidige protocol. Indien de ervaringen positief zijn, zal dit aangepast protocol ingevoerd worden.

Waarom wordt de persoon waarvoor ik zorg draag gevraagd om deel te nemen aan het project?
Alle bewoners van het Gielsbos die nu reeds medicatie krijgen voor het uitvoeren van tandheelkundige zorgverlening volgens het bestaande protocol en waarbij een behandeling gepland is in de periode tussen 9 december 2013 en 9 september 2014, worden uitgenodigd voor deelname aan dit project. Er zullen in totaal ongeveer 40 personen opgenomen worden in de studie.

Is er een verplichting om deel te nemen?

U beslist volledig vrijwillig of de persoon waarvoor u zorg draagt deelneemt of niet. Indien u beslist tot deelname, dan mag u deze informatiebrief behouden en vragen wij u om het toestemmingsformulier te ondertekenen (twee exemplaren). Eén toestemmingsformulier is bestemd voor de tandarts, het tweede exemplaar kan u bewaren. U heeft het recht om deelname te weigeren en het staat u vrij om op ieder moment en zonder opgave van een reden uit het project te stappen. Bij geval van weigering zal dit geen enkele invloed hebben op de kwaliteit van de zorgverlening aan de bewoner noch op de relatie met de behandelende tandarts, net zoals dit tot nu het geval is.

Wat houdt deelname aan het project in?
Bewoners met minstens 2 afspraken voor tandheelkundige behandeling zullen éénmaal behandeld worden met het bestaande protocol en éénmaal met het aangepaste protocol. Sommige personen zullen eerst het bestaande protocol en dan het aangepaste protocol ontvangen en bij anderen zal dit in omgekeerde volgorde gebeuren. Dit om de beoordeling van de effecten niet te beïnvloeden.

Tijdens de tandheelkundige verzorging zal de medewerking van de bewoner (hoe goed laat de bewoner toe om de tandverzorging uit te voeren) genoteerd worden. Aan de begeleiding zal gevraagd worden om het effect van de medicatie na de behandeling (slaperigheid, stemming, gedrag, eetlust,…) te noteren.

Wat zijn mogelijke risico's en ongemakken verbonden aan dit project?

De bewoner ontvangt tandheelkundige verzorging zoals gepland, enkel het soort medicatie dat in de voorbereiding gegeven wordt is verschillend. Er wordt in dit project op geen enkel ogenblik experimentele medicatie gebruikt of getest; het gaat om gekende producten die reeds lang toegepast worden in andere instellingen en situaties en waarvan de veiligheid en effectiviteit getest en gepubliceerd werd.

Worden de resultaten vertrouwelijk behandeld?

De gegevens die in het kader van deze studie verzameld worden, zullen uiterst vertrouwelijk behandeld worden. Hierbij wordt het medisch beroepsgeheim en de Belgische wetgeving nageleefd (onder meer de wettelijke vereisten zoals bepaald in de Belgische Wet van 11 december 1998 betreffende de bescherming van het privéleven, alsook de Belgische Wet van 22 augustus 2002 met betrekking tot de patiëntenrechten). Alle persoonlijke informatie wordt onder gecodeerde vorm opgeslagen; de identiteit van de bewoner zal op geen enkel moment kenbaar gemaakt worden aan onbevoegde derden.

Wat gebeurt er met de resultaten van het project?

Zodra het project afgesloten is, worden de resultaten meegedeeld en besproken met de betrokken verantwoordelijken van het Gielsbos. Bij positieve evaluatie zal het aangepaste protocol ingevoerd worden en zal dit toelaten de zorgverlening aan de bewoners te optimaliseren.

De resultaten van dit project zullen opgenomen worden in de masterthesis van de zorgverlenende tandartse, Mevr Ine Opsomer, in het kader van haar aanvullende opleiding Kindertandheelkunde en Bijzondere zorgverlening die zij volgt aan de KU Leuven.

Het is ook mogelijk dat de resultaten gepubliceerd worden in een tandheelkundig tijdschrift. Hierbij worden individuele gegevens op geen enkel ogenblik vrijgegeven en wordt de naam van de bewoner nergens vermeld. U kan aan ons vragen om een exemplaar van deze publicatie te ontvangen.

Kan er iets fout lopen?

In het kader van dit project wordt gebruik gemaakt van bestaande en geteste protocols. De toepassing ervan zal gebeuren met de grootste voorzichtigheid en nauwkeurigheid. Om die redenen is het hoogst onwaarschijnlijk dat de bewoner schade zou ondervinden die rechtstreeks dan wel onrechtstreeks verband houdt met het project. Vermits het project kadert in een thesis aan de KU Leuven, werd een verzekering afgesloten die eventuele schade opgelopen door deelname aan het project vergoedt conform de Belgische wet ter zake van 7 mei 2004.

Wie is de verantwoordelijke voor dit project?

Dit project is een samenwerking tussen het Gielsbos en de Dienst Tandheelkunde van de UZ/KU Leuven. Het project is een initiatief van tandarts Ine Opsomer, tandarts in het Gielsbos en tevens laatstejaars specialisatie-opleiding Kindertandheelkunde en Bijzondere zorgverlening aan de KU Leuven, en wordt uitgevoerd onder de leiding van Prof Dominique Declerck (Tandheelkunde, UZ/KU Leuven).

Het project werd uitgewerkt in overleg met de betrokken verantwoordelijken van het Gielsbos (artsen, directie, begeleiders).

Dit project werd goedgekeurd door de Commissie voor Medische Ethiek van de UZLeuven, wiens taak het is om na te gaan of aan alle voorwaarden betreffende veiligheid en vrijwaring van rechten wordt voldaan.

Indien u nog vragen heeft over dit project, aarzel dan niet contact op te nemen. Wij zullen u graag verder helpen.

Tandarts Ine Opsomer, Algemeen Tandarts (Gielsbos), Vosselaarseweg 1, 2275 Gierle (Lille)

Tel.nr: 014/60 12 11
E-mail: ine.opsomer@uzleuven.be

Dokter Jessy Leijer, Vosselaarseweg 1, 2275 Gierle (Lille)

Tel.nr: 014/60 12 11
E-mail: jessy.leijer@hetgielsbos.be

Dokter Gert Van Goethem, Vosselaarseweg 1, 2275 Gierle (Lille)

Tel.nr: 014/60 12 11
E-mail: gert.vangoethem@hetgielsbos.be

Directeur zorg - Guy Bruyninckx, Vosselaarseweg 1, 2275 Gierle (Lille)

Tel.nr: 014/60 12 11
E-mail: guy.bruyninckx@hetgielsbos.be

Prof. Dominique Declerck, Dienst Tandheelkunde, Opleiding Kindertandheelkunde en Bijzondere Zorgverlening, UZ/KU Leuven, Kapucijnenvoer 7 blok a bus 7001, 3000 Leuven

E-mail: dominique.declerck@med.kuleuven.be

TOESTEMMINGSFORMULIER

(exemplaar om te bewaren door toestemmingsverlener)

"Optimalisatie van medicamenteuze ondersteuning bij tandheelkundige zorgverlening aan personen met een mentale beperking"

	Gelieve aan te kruisen
1. Ik bevestig dat ik voldoende tijd heb gekregen om de informatie-brief te lezen en eventuele vragen te stellen. Mijn vragen in verband met deelname aan het project zijn voldoende beantwoord.	□
2. Ik kan de schriftelijke informatie behouden en ik behoud een kopie van de schriftelijke toestemmingsverklaring.	□
3. Ik begrijp dat de deelname van mijn kind/persoon waarvoor ik de zorg opneem aan dit project vrijwillig is en dat op elk moment kan beslist worden om uit het project te stappen zonder hiervoor een reden op te geven. De kwaliteit van de behandeling en de rechten als patiënt zullen niet door deze keuze beïnvloed worden.	□
4. Ik begrijp dat delen van het medisch dossier die van belang zijn voor het onderzoek ingekeken worden door personen die daarvoor bevoegd zijn. Ik geef toelating aan deze personen om het dossier in te kijken.	□
5. Ik ga akkoord met deelname aan deze studie.	□

Naam van de ***patiënt*** Handtekening

(voor instemming indien <18 jaar of verlengd minderjarig) Datum

Naam van de ***ouder of voogd*** Datum Handtekening

(voor toestemming indien <18 jaar of verlengd minderjarig)

Naam van de ***persoon die toestemming bekomt*** Datum Handtekening

Naam van de ***verantwoordelijke*** van de studie Datum Handtekening

TOESTEMMINGSFORMULIER

(exemplaar om te bewaren in dossier)

"Optimalisatie van medicamenteuze ondersteuning bij tandheelkundige zorgverlening aan personen met een mentale beperking"

	Gelieve aan te kruisen
1. Ik bevestig dat ik voldoende tijd heb gekregen om de informatie-brief te lezen en eventuele vragen te stellen. Mijn vragen in verband met deelname aan het project zijn voldoende beantwoord.	□
2. Ik kan de schriftelijke informatie behouden en ik behoud een kopie van de schriftelijke toestemmingsverklaring.	□
3. Ik begrijp dat de deelname van mijn kind/persoon waarvoor ik de zorg opneem aan dit project vrijwillig is en dat op elk moment kan beslist worden om uit het project te stappen zonder hiervoor een reden op te geven. De kwaliteit van de behandeling en de rechten als patiënt zullen niet door deze keuze beïnvloed worden.	□
4. Ik begrijp dat delen van het medisch dossier die van belang zijn voor het onderzoek ingekeken worden door personen die daarvoor bevoegd zijn. Ik geef toelating aan deze personen om het dossier in te kijken.	□
5. Ik ga akkoord met deelname aan deze studie.	□

Naam van de ***patiënt*** Datum Handtekening

(voor instemming indien <18 jaar of verlengd minderjarig)

Naam van de ***ouder of voogd*** Datum Handtekening

(voor toestemming indien <18 jaar of verlengd minderjarig)

Naam van de ***persoon die toestemming bekomt*** Datum Handtekening

Naam van de ***verantwoordelijke*** van de studie Datum Handtekening