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Challenges and need for support regarding the use of sedative drugs and sedation at the end of life in general palliative care: results from the mixed-methods study SedEoL

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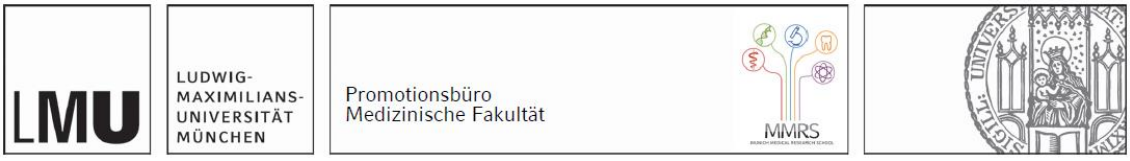

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Contents

List of abbreviations

List of publications

Paper I

Meesters S, Grüne B, Bausewein C, Schildmann E. "We don't want to sedate him" - A qualitative interview study on intentions when administering sedative drugs at the end of life in nursing homes and hospitals. *BMC Palliat Care*. 2021 Sep 13; 20(1): 141. doi: 10.1186/s12904-021-00832-0. PMID: 34517847; PMCID: PMC8439055.

Paper II

Meesters S, Grüne B, Bausewein C, Schildmann E. “Palliative Syringe Driver”? A Mixed-Methods Study in Different Hospital Departments on Continuous Infusions of Sedatives and/or Opioids in End-of-Life Care. *J Patient Saf*. 2021 Oct 13; 00(00). doi: 10.1097/PTS.0000000000000918.

Supplementary material

Grüne B, **Meesters S**, Bausewein C, Schildmann E. Challenges and Strategies Regarding Sedation at the End of Life in Hospitals and Nursing Homes. *J Pain Symptom Manage*. 2021 Dec 15; S0885-3924(21)00668-0. doi: 10.1016/j.jpainsymman.2021.12.012. Epub ahead of print. PMID: 34921935.

1. Individual contribution of the author

The author of this thesis contributed to the concept, design and conduct of the study. She was substantially involved in the development of the data extraction tool for quantitative data collection and in designing the interview guides for qualitative data collection. She jointly extracted quantitative data from patient and resident records and conducted interviews. With support of other team members and the project lead, the author defined the specific research questions for the publications of this thesis and prepared and analysed the data. She developed the concept of the publications and wrote the original manuscripts with critical revision of all authors. Furthermore, she was responsible for the publication process as corresponding author and was the main contributor to editing and reviewing the manuscripts. Regarding the third publication, included as supplementary material, she supported the first author in defining the research question, analysing the data and developing the concept. Moreover, she critically revised the manuscript and the revisions.

1.1 Contribution to paper I and paper II

Study concept and design: Schildmann E, Grüne B and Meesters S, with support of Bausewein C. Acquisition of data: Grüne B and Meesters S. Analysis of data: Meesters S, with support of Grüne B and Schildmann E. Interpretation of data: all authors. Drafting of the manuscript: Meesters S. Critical revision of the manuscript for important intellectual content: all authors.

1.2 Contribution to paper III (supplementary material)

Study concept and design: Schildmann E, Grüne B and Meesters S, with support of Bausewein C. Acquisition of data: Grüne B and Meesters S. Analysis of data: Grüne B, with support of Meesters S and Schildmann E. Interpretation of data: all authors. Drafting of the manuscript: Grüne B. Critical revision of the manuscript for important intellectual content: all authors.

2. Introduction

2.1 Comfort care and symptom control at the end of life in palliative care

Approximately two-thirds of all deaths in western countries occur due to or with a progressive disease.[1] Patients living with life-threatening diseases and their families face various physical, social, psychological and spiritual problems.[1] Palliative care aims at providing the best possible treatment and support for these patients and their families until death by preventing and relieving suffering within all areas named.[1, 2] It is provided in general and specialist settings: Specialist palliative care comprises services that provide predominantly palliative care, for example palliative care units or specialist palliative homecare teams. General palliative care includes care to patients with life-threatening diseases provided by primary care professionals, for example on general hospital wards.[2] While the palliative care approach generally aspires early integration in the disease process, it is especially of great importance in the dying phase to ensure comfort care and adequate symptom control. The use of sedatives is an important end-of-life measure when dying patients are suffering from intractable symptoms, such as pain, dyspnoea or anxiety.[3] When sedatives are used in a monitored way and with the intention to decrease or remove consciousness to relieve suffering from intractable symptoms, this is defined as “sedation in palliative care” or “palliative sedation”.[4] The reduction of consciousness can be administered temporarily or continuously (until death) and can range from mild to deep.[4] However, there is a wide variation in the definition of “sedation in palliative care” or “palliative sedation”.[5] Although it is an accepted treatment option at the end of life, it is controversially discussed in numerous empirical studies and ethical debates.[5-7] In the following, the terms “sedation in palliative care” and “palliative sedation” are equally referred to as “sedation”.

2.2 Prevalence of the use of sedatives and sedation

Empirical studies regarding the prevalence of the use of sedatives and sedation report very different results.[8, 9] According to systematic reviews, there is a wide variation of the prevalence of sedation reported, ranging from 12 to 67%.[10, 11] This wide range is firstly related to variations in study designs. While population-based surveys are based on clinicians’ accounts of the practice labelled as “sedation” by themselves, retrospective chart reviews generally assess the use of

sedatives independent of the label.[12-18] Moreover, comparison is often difficult, even for studies with similar study designs, due to the different operationalisation of the “sedation” or sedatives. Retrospective chart reviews include different drugs and modes of administration, and a vagueness in terms and different definitions may contribute to the wide range among surveys.[5, 6, 8, 13, 17, 18] Narrowing down the definition of sedation, for example, to situations in which sedation was primarily intended will generate a lower prevalence than that also including cases of reduction of consciousness as a side effect.[6] Furthermore, systematic reviews include studies examining different forms of sedation and it is not always clear whether the data refer to mild or deep, continuous or temporary sedation.[9] Irrespective of these methodological difficulties, the existing literature indicates differences in prevalence between countries as well as between general and specialist settings. Country-specific differences were shown among all settings and forms of sedation: according to a questionnaire study among Dutch, Flemish and British physicians, continuous deep sedation was significantly less often provided in Dutch hospitals (11%) compared to hospitals in Flanders (20%) and the U.K. (17%).[15] Reasonably comparable retrospective reviews reported a prevalence of continuous midazolam doses in patients at the end of life in palliative care units of 76% in Germany, 45% in Hong Kong and 22% in Canada.[13, 19, 20] The prevalence of sedative drug use in general hospital departments ranged from 16% in South Korea to 63% in Germany.[12, 18] Referring to setting-specific differences, various studies identified a higher prevalence of sedation and sedative drug use for specialist settings.[18-22] Moreover, the proportion of patients receiving sedatives and sedation seems to vary across institutions within the general setting, which may depend on the patient population, the physicians’ speciality and their experience.[12, 17, 18] Finally, a recent systematic review examining changing practices in the use of continuous sedation at the end of life concluded that the frequency of continuous sedation seems to increase over time. The review reported a prevalent increase over time from 3% in Denmark in 2001 to 18% in the Netherlands in 2015, possibly partly due to an extension of indications for sedation.[23]

2.3 Variations in terms, definitions, concepts and guidelines

Various terms have been used to refer to the use of sedatives at the end of life, including “terminal sedation”, “palliative sedation”, “palliative pharmacological sedation” and “intentional sedation”.[6, 8, 9, 24] Moreover, no common definition of these terms exists, and definitions and key terms are

mostly vague and partly pre-emptive.[5, 25] While some authors reported that all guidelines at least describe sedation consistently as the intended reduction of consciousness, a recent review extracted “reduced consciousness” as the only content shared in all definitions.[5, 9, 26] Europe-wide and numerous country-specific sedation guidelines aiming to set standards and promote best practice differ not only in their terms and definitions but also in key recommendations.[25-28] According to a recent systematic review, variance between guidelines was identified regarding the definition of the practice, indications for its use, continuation of life-prolonging therapies, medications used and timing/prognosis.[28] The timing of initiation, for example, ranges from “hours to days” to “a week” in different guidelines.[26, 28] Additionally, Schildmann and colleagues identified considerable variations in their systematic reviews concerning the concreteness of details.[25, 27] Accordingly, only a few guidelines, for example, state reasons for the distinction of somatic and psychological symptoms regarding the restriction of sedation to exceptional cases for psychological or existential suffering.[25] Differences in terms and concepts were not only described between studies and guidelines but also among healthcare professionals.[29, 30] Comparing different countries, various studies showed that healthcare professionals in the U.K. avoid the label “sedation”, preferring accounts of a settled or comfortable state. A reduction of consciousness was often described as a side effect of the medication used for managing difficult symptoms. Therefore, healthcare professionals in the U.K. perceived sedation mostly as a process rather than a single decision.[29, 31, 32] By contrast, healthcare professionals from Belgium and the Netherlands defined sedation predominantly as an intentional reduction of consciousness. They emphasised that sedation is an explicit medical decision.[29, 31] Respondents from the Netherlands partly described sedation and euthanasia as alternatives.[29, 31] Comparing settings, a study from Switzerland revealed that the understanding of continuous deep sedation until death differs between healthcare professionals from general and specialist settings.[30] In addition to a lack of consistent terminology and definitions, the study described differences in the understanding of common terms as well as regarding indication and intentions. While specialist palliative healthcare professionals, for example, mostly defined continuous deep sedation until death as an explicitly intended measure to treat refractory symptoms, healthcare professionals in general palliative care perceived deep sedation also as a side effect of increased pain medication.[30] Differences in terms, definitions, concepts and guidelines can cause problems from both a theoretical and practical perspective.[5, 6, 30] Firstly, as shown in the previous chapter, variety

and vagueness are considered as contributing causes for the inconsistencies in empirical data described, hindering comparisons of the sedation practice.[5, 6] Secondly, transparent and effective discussions and decision-making processes in practice require common terms with consistent understanding. If terms mean different things to different professions, breakdowns in communication may result, jeopardizing sufficient symptom control for patients.[5, 30] Various studies described a need to resolve the conceptual confusion, encompassing uniform definitions and a consistent understanding of these terms and definitions.[5, 6, 33]

2.4 Description of sedation practices

2.4.1 Variations in sedation practices

As shown above, existing guidelines differ considerably in their key recommendations. Accordingly, several studies also reported considerable variations in the sedation practice between countries, settings, and medical specialities. Reported variations refer to the prognosis of patients receiving sedation, indications, titrating and decision-making processes.[21, 23, 30, 31, 34, 35] Moreover, Seymour and colleagues identified differences in the values and concerns regarding consciousness during dying, hastening death, continuous sedation as an ‘alternative’ to euthanasia and using guidelines for practice as explanatory factors for the variations.[31] Referring to the value of consciousness, for example, healthcare professionals from the U.K. were reported to predominantly use low doses of sedatives, ensuring that patients could maintain interaction for as long as possible. By contrast, healthcare professionals from Belgium put more emphasis on the importance of adequately relieving the patient’s suffering and described, therefore, predominantly the use of deep sedation.[31]

2.4.2 Indications for the use of sedatives and sedation

Guidelines generally restrict the use of sedation at the end of life to symptoms, which are refractory to other symptom control measures to relieve intolerable suffering.[4] While many healthcare professionals, particularly from specialist settings, emphasise the use of continuous deep sedation restrictively for refractory and intolerable symptoms, empirical studies also describe deviations from this guideline recommendation.[29, 36-38] Moreover, the determination of refractoriness and intolerability seems to be challenging for practitioners and there appears to be room for improvement regarding tools for assessment.[30, 34, 38] Indications reported to require

sedation are mostly categorised in physical and psychological or existential symptoms. Most quantitative studies describe physical symptoms to indicate sedation, comprising dyspnoea, agitation, delirium and pain.[23, 34] Psychological or existential suffering is only rarely stated as an indication for sedation but reported to be co-present in many cases.[34] Qualitative interview studies revealed that healthcare professionals perceive physical and psychological or existential symptoms as interwoven, which together cumulate into states considered as refractory and intolerable.[38, 39] Moreover, social and practical factors, for example, the patient's personality, values and beliefs, seem to influence the decision to start continuous deep sedation in addition to medical indications.[38]

2.4.3 Drugs used for sedation

Guidelines consistently recommend benzodiazepines, neuroleptics/antipsychotics, barbiturates, and general anaesthetics for sedation at the end of life and exclude the use of opioids.[4] Systematic reviews identified midazolam as the main sedative drug used. Other frequently used sedative drugs include phenobarbital, promethazine and propofol.[23, 34] In contrast to guideline recommendations, several studies showed that opioids are also used as the only medication for sedation, particularly in the general palliative care setting.[23, 37, 40, 41]

2.5 Challenges and ethical reflections

Rietjens and colleagues stated in a recent publication that sedation is among the most challenging topics in end of life care.[7] Firstly, these challenges refer to the variations in terms, definitions and concepts described, affecting the evidence base and development of guidelines. Secondly, sedation is also a challenging topic in everyday practice. Continuous deep sedation until death is particularly surrounded by numerous ethical debates, as it constitutes the end of a person's social life.[9, 42] One major challenge is the differentiation between euthanasia and sedation. There is still extensive debate regarding the distinction between sedation and euthanasia in the literature as well as in practice.[21, 31, 43-45] A common argument used to distinguish sedation from euthanasia is that sedation does not shorten life.[43, 45] In addition to this empirical argument of differentiation, the appeal to Aquinas' Doctrine of Double Effect is often used to differentiate sedation from euthanasia on an ethical basis.[43, 44] Aquinas' Doctrine of Double Effect includes four aspects: (1) the action is not bad in itself; (2) only the good effect is intended, the bad one is merely foreseen;

(3) the bad effect is coincidental; and (4) the good effect outweighs the bad effect.[43] However, there is no consensus regarding these arguments.[46] Beyond these arguments discussed in the literature, physicians and nurses morally justify the use of sedation with the arguments of 'last resort', 'sanctity of life', 'autonomy' and 'proportionality'.[42] Despite these morally justifications and many studies which indicate no life-shortening effect of sedation, uncertainties regarding the differentiation and concerns regarding the hastening of death are highly prevalent among healthcare professionals.[32, 47-48]. In addition to these major challenges, studies reported further challenges regarding indication and timing, the effectiveness of sedation, insufficient education and experience, interaction within the team or the family, and organisational barriers.[48-52] Healthcare professionals described, for example, difficulties in clearly identifying and interpreting symptoms with fears of being influenced by their own emotions.[50-51] As continuous deep sedation especially is not a routine practice, many healthcare professionals do not feel adequately educated and experienced, particularly in finding the right dose.[50] Moreover, there seem to be uncertainties regarding the effectiveness of sedation because it is questionable whether putting people to sleep provides relief automatically.[51] Qualitative studies showed that problems in communication and interaction within the team and with the family can cause difficulties and moral distress.[50, 52] Reported problems include, for example, pressure from team members or the family, unclear roles and diverging opinions.[52] Organisational barriers were only rarely described and referred mainly to the unavailability of medication.[50] These uncertainties and concerns seem to differ between healthcare professions, which could partly be explained by differences regarding the experience with specialist palliative care and sedation as well as by different role models.[32, 48]

2.6 Description of the mixed-methods study: sedation at the end of life outside specialist palliative care (SedEol)

Both publications of this thesis are based on research results from the SedEoL study, a multicentre mixed-methods study on the use of sedatives and sedation at the end of life outside specialist palliative care. As described, sedation at the end of life is an accepted but much debated and challenging practice. Most research on sedation has been conducted in the specialist setting. However, international studies show that sedation at the end of life also takes place in settings outside specialist palliative care, i.e. hospital departments or nursing homes.[14, 22, 35, 53-54] Research

results from the general palliative care setting are needed as only a minority of about 4% of people die in specialist palliative care settings.[55] Moreover, international research results demonstrate that the understanding of sedation at the end of life and the practice are highly dependent on the ethico-legal framework and the health system.[31, 56-57] Therefore, research results from other countries cannot readily be transferred to the German health care context and research results from Germany on this topic are scarce. Finally, existing studies focus primarily on the practice of continuous deep sedation until death. Other sedation practices taking place in hospitals or nursing homes are only rarely taken into account.[31, 57] Therefore, SedEoL aimed to describe the current practice of sedation during the last seven days of life outside specialist palliative care in selected German hospital wards and nursing homes and to explore associated challenges, as perceived by non-specialist healthcare professionals, and possible measures of support.

The specific research questions were:

(1) What are the frequencies and characteristics of different types of sedation during the last seven days of life outside specialist palliative care in selected hospital departments and nursing homes?

(2) What are healthcare professionals' views, experiences and perceived challenges regarding different types of sedation at the end of life outside specialist palliative care settings?

(3) Which identified challenges of sedation at the end of life outside specialist palliative care are addressed in published sedation guidelines, and which adaptations of guidelines are necessary for clinical contexts outside specialist palliative care in the light of the empirical findings of the study?

To address these aims, a sequential mixed-methods design, including an exploratory chart review followed by qualitative interviews and focus groups, was conducted. The quantitative part comprised 1032 records of patients/residents who died between January 2015 and December 2017 (n = 517 in hospital departments, n = 512 in nursing homes). Regarding the qualitative part, 25 nurses (n = 13 from hospital departments, n = 12 from nursing homes) and 24 physicians (n = 12 from hospital departments, n = 12 from nursing homes) participated in the interviews between April and October 2019. The two focus groups took place in July 2020 and consisted of 14 participants (five nurses, six physicians and three NA/both). The study results are expected to inform future research and guideline development regarding sedation at the end of life outside

specialist palliative care and identify the need for support and possible measures for healthcare professionals.

2.7 Objectives and contents of this thesis

The overarching aim of this thesis was to identify the challenges and need for support regarding the use of sedatives and sedation at the end of life in German general palliative care both quantitatively and qualitatively. The third publication, included as supplementary material, provides an overview of all challenges perceived by the healthcare professionals of the participating centres. The two publications included in this thesis focused on specific aspects, which were described in more detail. The first publication explored the concept of sedative drugs and intentions when administering sedative drugs, including comparisons between nurses and physicians and between healthcare settings. The second publication studied continuous infusions of sedatives and/or opioids in hospital departments.

The research questions of the included publications are stated and chapters are summarised briefly in the following. In addition to the publications included in this thesis and provided as supplementary material, the team members published three further papers describing the quantitative research results.[17, 18, 62]

Chapter 5 refers to a qualitative study exploring what concept German healthcare professionals in general palliative care have of “sedative drugs”. Moreover, the study examines the intentions with which healthcare professionals administer sedative drugs at the end of life. We conducted interviews with 24 physicians and 25 nurses. The transcripts of the semi-structured interviews were analysed thematically with MAXQDA, following the Framework approach. The results demonstrated that German healthcare professionals in general palliative care define different drugs as sedative drugs. Most interviewees described to use benzodiazepines, antipsychotics, or opioids when sedative drugs are necessary, some also named sleeping medication, antiemetics, and analgesics in general. Only few interviewees divided the drugs into different medication groups, referring to sedative drugs, anxiolytics, analgesics, and others. When being asked with which intentions they administer sedating drug, most interviewees described the exclusion of intentions, that is, what they want to avoid. The term “sedation” was mostly used for inducing unconsciousness, and our interviewees stated that they generally do not induce deep reductions

of consciousness. To accept a side effect rather than making an explicit decision and avoidance of the term “sedation” have important consequences. Healthcare professionals will probably not refer to respective guidelines, and the decision-making process and informed consent of the patient may be impeded. The results provide relevant information for the structuring of educational courses in general palliative care: Healthcare professionals need to understand the difference between sedation as side effect and intentional sedation as well as the potential transition. Moreover, it is important to address negative associations with the term. Consequently, adherence to guidelines can be promoted and transparent and clear communication can be enabled.

Chapter 6 refers to a mixed-methods study assessing the use of continuous infusions of sedatives and/or opioids within the last week of life in general hospital departments. For the quantitative part, we analysed data of the retrospective chart review to describe the current clinical practice. Additional to descriptive statistics, we conducted bivariate analysis to evaluate differences between patients receiving continuous infusions of sedatives and/or opioids and patients not receiving them as well as between hospital departments. We used qualitative data to explore how healthcare professionals experience the use of continuous infusions of sedatives and/or opioids. We analysed the transcripts of the semi-structured interviews thematically utilising the Framework approach. For data analysis and interpretation, we integrated both phases with equal weight. Quantitative results were explained by qualitative results or we compared the results to each other. During the last week of life 359/517 (69%) patients received a continuous infusion of sedatives and/or opioids on at least one day. Although many interviewees stated that they start continuous infusions of sedatives and/or opioids only in cases of substantial suffering, data suggest that the label “palliative” may be a relevant factor for starting continuous infusions. It is likely that some physicians only start continuous infusions of sedatives and/or opioids when the change in treatment goal from curative to palliative is documented. Additionally, it can be assumed that the administration might be a form of standard procedure in the final phase of patients. Thus, the possible requirement of the label “palliative” to administer continuous infusions can lead to the avoidance or postponement of continuous infusions. Furthermore, a possible standard procedure poses the risk of using continuous infusions by default without individually assessing indications and patient’s needs. In conclusion, there is a need to include symptom control with continuous infusions in recommendations and programmes for general palliative care.

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3. Zusammenfassung:

In der Sterbephase können unerträgliche und therapierefraktäre Symptome auftreten, darunter Schmerzen, Atemnot, Angst oder Unruhe. Sedierung ist in diesen Situationen eine grundsätzlich akzeptierte Handlungsoption. Jedoch deuten zahlreiche ethische Diskussionen sowie eine große Anzahl an empirischen Forschungsarbeiten darauf hin, dass es sich bei Sedierung am Lebensende um ein komplexes und herausforderndes Konzept handelt. „Sedierung in der Palliativversorgung“ oder „palliative Sedierung“ kann als überwachter Einsatz von Medikamenten definiert werden mit dem Ziel, das Bewusstsein zu vermindern oder aufzuheben, um die Symptomlast in anderweitig therapierefraktären Situationen zu reduzieren“. Jedoch fehlt es an einer einheitlichen Terminologie und Definition sowie an einheitlichen Empfehlungen in Leitlinien. „Sedierung“ wird dementsprechend für verschiedene Vorgehensweisen verwendet, was zu Herausforderungen sowohl in der Praxis als auch in der Literatur führt. Neben dieser Begriffsverwirrung ist Sedierung am Lebensende vor allem im praktischen Alltag von weiteren Herausforderungen begleitet, darunter zum Beispiel die Abgrenzung zur Sterbehilfe oder Schwierigkeiten bei der Indikationsstellung. Bisher fokussieren sich Studien zu Sedierung am Lebensende vorrangig auf das spezialisierte Setting. Da jedoch der Anteil an Menschen, die in Settings der spezialisierten Palliativversorgung versterben, gering ist, sind Forschungsergebnisse aus dem Setting der allgemeinen Palliativversorgung nötig.

Ziel dieser Arbeit ist es, Herausforderungen und Unterstützungsbedarf bei der Anwendung von sedierenden Medikamenten und Sedierung in der allgemeinen Palliativmedizin in Deutschland zu untersuchen. Der erste Artikel untersucht qualitativ das Konzept, das Versorgende von „sedierenden Medikamenten“ haben sowie die Intentionen, mit denen sedierende Medikamente verabreicht werden. Der zweite Schwerpunkt liegt auf der Verabreichung kontinuierlicher Infusionen mit Sedativa und/oder Opioiden im Krankenhaus. Mit Hilfe eines Mixed-Methods Ansatzes wurde quantitativ die Praxis und qualitativ erlebte Erfahrungen untersucht.

Als Datenquelle für die Artikel wurden Daten aus der SedEoL Studie genutzt, eine explorative Mixed-Methods Studie, die den Einsatz sedierender Medikamente und Sedierung am Lebensende in der allgemeinen Palliativversorgung untersucht. In einem sequentiellen Design wurde im ersten Schritt eine retrospektive Aktenanalyse durchgeführt. Insgesamt wurden 1032 Akten von Patient*innen und Bewohner*innen untersucht, die zwischen Januar 2015 und

Dezember 2017 auf den teilnehmenden Krankenhausstationen und in Pflegeheimen verstarben. Im nachfolgenden qualitativen Teil wurden 25 Pflegende und 24 Ärzt*innen aus den teilnehmenden Krankenhausstationen und Pflegeheimen semi-strukturiert interviewt. Die quantitativen Daten wurden mittels deskriptiver statistischer Analyse ausgewertet, die qualitativen Daten mittels Framework Analyse.

Die Ergebnisse des ersten Artikels zeigten, dass es kein einheitliches Konzept von sedierenden Medikamenten unter den Befragten gibt. Die meisten nannten Benzodiazepine, Opioide und Antipsychotika. Jedoch ordneten einige die genannten Medikamentengruppen insgesamt unter sedierenden Medikamenten ein, während andere zwischen sedierenden Medikamenten, Anxiolytika und Analgetika unterschieden. Bezüglich der Intention für die Verabreichung sedierender Medikamente hoben die Befragten insbesondere hervor, was sie nicht erreichen möchten. Durch den Einsatz sedierender Medikamente soll das Leiden der Patient*in reduziert werden, eine Bewusstseinsreduktion ist aber in der Regel nicht beabsichtigt und wurde hauptsächlich als Nebeneffekt wahrgenommen. Außerdem wurde der Begriff „Sedierung“ vorwiegend mit tiefer Bewusstseinsreduktion assoziiert, die es zu vermeiden galt. Während es für die Befragten von großer Bedeutung war, dass sedierende Medikamente nicht zur Ruhigstellung oder Fixierung verwendet werden, erwähnten sie auch, dass die Medikamente möglicherweise zur Beruhigung der Angehörigen und des Teams verwendet werden. Abschließend berichteten die Befragten, dass eine Lebensverkürzung niemals Ziel des Einsatzes sein darf, man einen möglichen lebenszeitverkürzenden Effekt jedoch ab einer gewissen Dosierung in Kauf nehmen muss. Die Untersuchung von kontinuierlichen Infusionen mit Sedativa und/oder Opioiden zeigte, dass 69% der verstorbenen Patient*innen in den letzten sieben Lebenstagen diese Behandlung erhielten, wobei Midazolam (99%) und Morphin (80%) die am häufigsten eingesetzten Medikamente waren. Die Interviewten berichteten, dass kontinuierliche Infusionen mit Sedativa und/oder Opioiden nur bei entsprechendem Leiden eingesetzt werden. Jedoch zeigten sich Hinweise darauf, dass es einen Zusammenhang zwischen der Bezeichnung „palliativ“ und dem Ansetzen der Infusionen gibt. Zum einen wurden diese teils als „Palliativ-Perfusor“ bezeichneten Infusionen in einigen Fällen als Standardbehandlung für sterbende Patient*innen verstanden. Zum anderen schienen Ärzt*innen im Ansetzen der kontinuierlichen Infusionen zurückhaltend zu sein, wenn die Bezeichnung „palliativ“ nicht in der Akte vermerkt war. Der spezialisierte Palliativdienst wurde bei 60% aller Patient*innen mit kontinuierlicher Infusion mit Sedativa

und/oder Opioiden hinzugezogen und auch in den Interviews als elementare Unterstützungsstrategie benannt.

Zusammenfassend zeigen die Ergebnisse der Artikel deutlich, dass es in der allgemeinen Palliativversorgung Unterstützungs- und Schulungsbedarf bezüglich der Anwendung von sedierenden Medikamenten und Sedierung am Lebensende gibt. Schulungsbedarf existiert in Bezug auf das Konzept von sedierenden Medikamenten und Sedierung. Eine explizite Benennung als Sedierung anstelle der Inkaufnahme der Bewusstseinsreduktion als Nebeneffekt kann die Anwendung von entsprechenden Leitlinien fördern und zu einem bewussten und informierten Entscheidungsprozess beitragen. Daran schließt sich ein genereller Schulungsbedarf bezüglich Möglichkeiten der Palliativversorgung an. Die Behandlung mit kontinuierlichen Infusionen mit Sedativa und/oder Opioiden sollte weder standardmäßig für sterbende Patient*innen angesetzt noch mit palliativer Versorgung gleichgesetzt werden. Andererseits sollten Wissen und Erfahrung bezüglich sedierender Medikamente ausreichend vorhanden sein, um einen verzögerten Einsatz aufgrund von Unsicherheiten und Bedenken zu verhindern.

4. Abstract (English):

In the dying phase, unbearable and therapy-refractory symptoms may occur, including pain, dyspnoea, anxiety or agitation. Sedation is a generally accepted treatment option in these situations. However, the numerous ethical discussions as well as a substantial amount of empirical research indicate that sedation at the end of life is a multifaceted and challenging concept. "Sedation in palliative care" or "palliative sedation" can be defined as the use of medication in a monitored way and with the intention to decrease or remove consciousness to relieve suffering from intractable symptoms. However, there is a lack of uniform terms and definitions as well as uniform recommendations in guidelines. "Sedation" accordingly includes different procedures, which leads to challenges both in practice and in the literature. In addition to this confusion of terms, sedation at the end of life is accompanied by further challenges, especially in practical everyday life, including the differentiation from euthanasia or difficulties in determining indications. So far, studies on sedation at the end of life focused primarily on the specialist palliative care setting. As the proportion of people who die in specialist palliative care settings is rather small, research findings from the general palliative care setting are needed.

The aim of this thesis is to identify the challenges and need for support regarding the use of sedatives and sedation in general palliative care in Germany. The first publication qualitatively examines what concept German healthcare professionals in general palliative care have of “sedative drugs” and the intentions with which healthcare professionals administer them at the end of life. The second publication focuses on the administration of continuous infusions of sedatives and/or opioids in hospital departments. Using a mixed-methods approach, we examined the practice quantitatively and experiences qualitatively.

Data were taken from the results obtained in the SedEoL study, an exploratory mixed-methods study investigating the use of sedative drugs and sedation at the end of life in general palliative care. A retrospective chart review was followed by qualitative semi-structures interviews. A total of 1032 records of patients and residents who died in the participating hospital departments and nursing homes between January 2015 and December 2017 were examined. Subsequently, 25 nurses and 24 physicians from the participating hospital departments and nursing homes were interviewed. We used descriptive statistical analysis to analyse de quantitative date and utilised the Framework Analysis to analyse the qualitative data.

The results of the first publication showed that there is no uniform concept of “sedative drugs” among the interviewees. Most interviewees described to use benzodiazepines, antipsychotics, or opioids when sedative drugs are necessary, some also named sleeping medication, antiemetics, and analgesics in general. With regard to the intention for administering sedative drugs, most interviewees described the exclusion of intentions, that is, what they want to avoid. The use of sedative drugs was intended to reduce the patient's suffering, but a reduction of consciousness was generally not intended and was primarily perceived as side effect. In addition, the term “sedation” was mainly associated with a deep reduction of consciousness, which should be avoided. While it was of great importance to the interviewees that sedative drugs are not used for tranquilizing or restraining the patient, they also mentioned that the drugs may partly be used to relieve the relatives' and the team's situation. Finally, the interviewees reported that shortening life must never be the aim but acknowledged that a life-shortening effect might result from high doses of sedative drugs. The second publication showed that 69% of the deceased patients received a continuous infusion of sedatives and/or opioids in the last seven days of life, with midazolam (99%) and morphine (80%) being the most frequently used drugs. The interviewees reported to use continuous infusions of sedative drugs and/or opioids only used in cases of serious suffering. However, data suggest that the label “palliative” may be a relevant factor for starting continuous infusions. In some cases, the continuous infusions, sometimes referred to as "palliative syringe driver", may be perceived as standard treatment for dying patients. Moreover, physicians seemed to hesitate starting the continuous infusions before the term "palliative" was recorded. The specialist palliative care service was consulted in 60% of all patients with continuous infusions of sedatives and/or opioids and was also mentioned in the interviews as elementary support measure.

In conclusion, the results of the two publications clearly show that there is a need for support and training in general palliative care regarding the use of sedative drugs and sedation at the end of life. First, healthcare professionals need to be educated regarding the concept of “sedative drugs” and sedation. Explicitly naming sedation instead of accepting the reduction of consciousness as a side effect can promote the use of appropriate guidelines and contribute to a conscious and informed decision-making process. Moreover, there is a need for training in palliative care methods. Treatment with continuous infusions of sedatives and/or opioids neither should be standard for dying patients nor equated with palliative care. Conversely, knowledge and

experience regarding sedative drugs should be sufficient to prevent delayed use due to uncertainties and concerns.

5. Paper I

“We don’t want to sedate him“ – A qualitative interview study on intentions when administering sedative drugs at the end of life in nursing homes and hospitals

Published in:

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Meesters S, Grüne B, Bausewein C, Schildmann E

Meesters, S., Grüne, B., Bausewein, C. Schildmann, E. “We don’t want to sedate him” - A qualitative interview study on intentions when administering sedative drugs at the end of life in nursing homes and hospitals. BMC Palliat Care 20, 141 (2021). https://doi.org/10.1186/s12904-021-00832-0

6. Paper II

“Palliative syringe driver”? – A Mixed-Methods Study in Different Hospital Departments on Continuous Infusions of Sedatives and/or Opioids in End-of-Life Care

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Meesters S, Grüne B, Bausewein C, Schildmann E. "Palliative Syringe Driver"? A Mixed-Methods Study in Different Hospital Departments on Continuous Infusions of Sedatives and/or Opioids in End-of-Life Care. J Patient Saf. 2022 Jun 1;18(4):e801-e809. doi: 10.1097/PTS.0000000000000918. PMID: 35617602; PMCID: PMC9162073.

Supplementary material: Paper III

Challenges and Strategies Regarding Sedation at the End of Life in Hospitals and Nursing Homes

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