Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences

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How is the practice for intrathecal analgesia and palliative sedation with propofol in Norwegian palliative care units?

Master's thesis in Clinical Health Science, specialisation in pain and palliative care

Supervisor: Olav Magnus Fredheim

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ABSTRACT

Background: Pain is a predominant symptom for many patients with advanced stage cancer, and present in almost everyone towards the end of their life. Intrathecal administration of analgesics may provide a feasible option for patients who experience pain so severe it is intractable to standard analgesic regimens. In cases where pain or other symptoms towards the end of life are so severe that they are refractory to standard treatments, palliative sedation may be warranted. The anaesthetic agent propofol has been proposed as a last resort for this purpose when other agents fail to provide relief. Purpose: The aim of this study was to map the practice for intrathecal analgesia and palliative sedation with propofol in Norwegian palliative care units and compare findings to research literature available. Material and methods: Information about the practise for these two advanced anaesthesiologic treatment modalities were collected through a questionnaire directly from the palliative care units. An extensive search in scientific databases was carried out to find research literature. Results and conclusion: Most hospitals can offer their patients intrathecal pain treatment and about a third of the units have carried out palliative sedation with propofol within the last two years. Variances are found in frequency, choice of medications and monitoring of the patient. The total number of patients receiving these treatments are low, possibly indicating that more patients could have benefited from these anaesthesiologic methods. The variances in practice surrounding intrathecal analgesia and palliative sedation with propofol portray a need for further studies to establish better evidence.

RELEVANCE

This study is relevant as there is a lack of evidence on how and when intrathecal analgesia should be initiated, and little or no documentation on how palliative sedation with propofol should be performed. This is health care assessment research, and provides indications that further research into this field is required. Research is needed to establish evidence for best practice, however in the meanwhile there would be an advantage to establish consensus-based guidelines to ensure safe and effective treatment of the patients in need of these treatments.

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BACKGROUND

Introduction

Pain is one of the most feared symptoms in cancer patients (1-7). It is a symptom in two thirds of all patients with advanced stages of cancer, and in almost everyone the last 48 hours of life (1-7). 10-15% of these patients do not receive adequate pain relief with standard treatment based on WHO's guidelines for treating cancer pain in adults. The impact of pain can be profound when inadequately controlled (1-9). WHO's recommendations for treating cancer pain in adults are illustrated through a three step 'ladder' with the first step being non-opioids (paracetamol, ASA or NSAIDs), second step adding weak opioids and third step adding strong opioids. All steps may include adjuvants such as steroids, anxiolytics or antiepileptics (10). Oral opioids are the foundation of cancer pain management; however, they have their limitations with regards to side effects. Increasing evidence displays that the use of interventional techniques improve pain experience, and may possibly also increase survival (11, 12). Many researchers have consequently suggested to expand WHO's pain ladder with a fourth step that opens for interventional techniques in treating refractory cancer pain (2, 3, 7, 13). Although no fourth step is in place, the WHO guidelines open for nerve-blocks if adequate pain control is not obtained by the three-step ladder (10). Interventional pain management would include nerve-blocks, one of which could be a neuraxial-block.

Patients with pain refractory to standard treatment, may respond well to neuraxial administration of medications where local anaesthetics and/or opioids can be delivered into either the epidural or intrathecal space (1, 6, 13-15) (fig. 1). Intrathecal injections are based upon medication delivery close to afferent nociceptive fibres and ascending tracts. The medications act upon opioid receptors and sodium channels, which along with NMDA receptors and calcium channels are involved in pain transmission and modulation (5). Opioid receptors are found in peripheral tissues, dorsal horn and several areas of the brain. Intrathecal administration of morphine in humans was documented for the first time by Wang et al. in 1978, reporting significant reduction in pain levels without unacceptable side effects (12). Later studies have also demonstrated reduction in pain scores, drug toxicity and oral opioid requirements compared to standard treatment (1, 12). Intrathecal drug delivery is a feasible

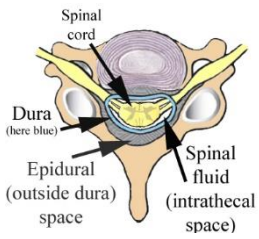


Fig. 1

treatment strategy for both neuropathic and nociceptive pain, but it is important to note that not all patients are appropriate candidates for this treatment option (16). Comorbidities related to the disease, psychosocial factors and life expectancy should be evaluated carefully before deciding to proceed with intrathecal techniques (16). Anticoagulation, active infections, bleeding diathesis and long-term neurologic deficits may be contraindications (17). Cancer patients with pain refractory to standard treatments are often considered for intrathecal treatment too late in the course of the disease, which can make them less suitable candidates for this treatment option (12). Intrathecal drug delivery can be done via an implantable- or an external pump. Early implantation of an intrathecal drug delivery system has been associated with prolonged survival rates, better analgesia and reduced drug-related adverse effects compared to oral and parenteral medications alone (5, 12).

Satisfactory symptom relief is central in all medical care (18). Health care professionals have a moral and medical obligation to eagerly address pain and other intolerable symptoms for patients with advanced cancer (18). Some patients will have so severe end-of-life symptoms such as pain, profound respiratory distress or agitation the last few hours or days of their life, that they are refractory to typical therapeutic regimens and the only course of action is to reduce the patient's level of consciousness so that he/she cannot perceive the distress. This treatment is known as palliative sedation or end-of-life-sedation and is well recognized and accepted for this group of patients who would otherwise suffer immensely at the end of their life (19-23).

Palliative sedation therapy is used mainly in the last hours or days of the patient's life, and should not hasten death, in contrast to euthanasia (21, 24). Although limited evidence is available, existing studies find that neither the administration of palliative sedation nor the degree of sedation hastens death in otherwise terminally ill patients (18).

There is yet no consensus on which medications should be used for palliative sedation nor the appropriate level of monitoring (23). There is a lack of trials that evaluates the use of sedating agents for this specific application. This may leave palliative care providers to depend upon outdated or insufficient information, or rely on the manufactures recommendations for dosing and administration which most likely are intended for other uses than palliative sedation (19). The current published guidelines on palliative sedation are of limited quality with regards to

medications and monitoring (23). Several studies have found large differences from provider to provider in sedation rates, possibly due to a lack of authorative guidelines and consensus in this field, and further research is called for (25, 26).

Aim

Intrathecal administration of analgesia and palliative sedation with propofol are two separate treatment modalities, however they are both advanced anaesthesiologic treatment methods traditionally used in surgical settings where the patient is observed and monitored by an anaesthesiologist or nurse anesthetist with all necessary monitoring and airway equipment easily available. Both treatments have been taken into use in palliative medicine when symptom relief is not obtained by standard treatment regimens. Intrathecal analgesia is initiated in advanced stages of cancer, but where the patient still has a life expectancy of weeks or months (or even longer), whereas palliative sedation is used in the terminal setting where life expectancy is only hours or days. It is a rarity that these two treatments are used at the same time, although it is possible that a patient with an ongoing intrathecal infusion also will be in need of sedation at the last hours of his life. The aim of this thesis is to explore the practice for use of intrathecal analgesia and palliative sedation with propofol in Norwegian palliative care units and compare the findings to published literature. Although there are many aspects to these treatment modalities, including important ethical considerations for patient and next of kin, this thesis will focus on frequency in which these methods are used and patients safety measures in connection with monitoring and hospital care level. With a lack of documentation on how intrathecal pain treatment and palliative sedation with propofol are best being managed, there is likely to be large varieties in how these options are employed around the country. Even though differences may be due to relevant local conditions, it may be reasonable to assume that large dissimilarities in clinical practice indicate that there is a need for further research and national guidelines for these treatment options.

Research question

The overall research question *"How is the practice for intrathecal analgesia and palliative sedation with propofol in Norwegian palliative care units?"* will be addressed by answering the following specific research questions:

- When standard pain treatment as recommended by the WHO fails to provide satisfactory pain relief, which other analgesic options does the units often try before considering intrathecal analgesia?
- Which medications are most frequently used for intrathecal analgesia?
- How is the units' practice for reduction of systemic opioids after initiation of intrathecal analgesia?
- Where is intrathecal treatment initiated and at which care level is the patient being monitored during and after the procedure of implanting the catheter?
- What proportion of the palliative units have used propofol for palliative sedation the last two years?
- Where is the patient when palliative sedation with propofol is initiated and which vital parameters are being monitored during the sedation?
- Which health care professionals are responsible for assessment of vital parameters and titration of drug dosing during palliative sedation with propofol?

Theoretical background

Interventional pain management

Interventional pain management can be an option when pain is refractory to standard treatments (27). These techniques are often invasive and require access to specialist nursing and interventional pain specialists (27). It may include neuraxial analgesia (delivery of medications into the epidural or intrathecal space), peripheral nerve-blocks, plexus-coeliac-blocks or chordotomies, but in palliative medicine intrathecal analgesia is the most frequently used method (27). Hawley et al. (13) report that the effectiveness of intrathecal infusions has been documented by large case series and one randomised trial, and has since 1999 been considered the next treatment step for cancer patients with pain refractory to WHO's three step ladder. Still, in many countries this intervention is rarely available. It might be many reasons for this diversity in clinical practice, including unfamiliarity with the intervention, lack of anaesthesia resources in palliative care and financial concerns (13). Due to the rarity of intrathecal analgesia, it is often considered an 'extraordinary measure' conflicting with the traditional minimally invasive palliative care philosophy (13). Kurita et al. (15) have done a systematic review of the efficacy of spinal opioids in connection with an initiative to revise the European Association for Palliative Care guidelines on the use of opioids for cancer pain. They report that spinal opioid therapy may be efficient for patients with intractable pain, although the review showed that the present evidence for this intervention is very weak meaning firm conclusions cannot be made and there is a need for renewed research activity on this topic (15). This conclusion has however been strongly criticised by Breivik (8) as he argues there is evidence displaying the efficacy of intrathecal analgesia for this patient group, and claiming one reason for the negative conclusion of Kurita et al. were that they only focused on opioids without the addition of local anaesthetics.

Treatment options before intrathecal drug delivery

Patients should have received an optimal trial of analgesics as described by WHO's pain ladder before considering intrathecal treatment (5, 16). Some authors suggest contemplating a diagnostic single bolus trial to explore effectiveness before implanting a catheter (5, 28). There is some debate over the usefulness of a trial given the difficulty in generalising long-term effect from a short period of drug exposure, and the need for rapid pain relief in patients with short

life expectancy. Trialling of opioids might also be problematic due to route conversion issues and the probable need for dose reduction of systemic opioids, both of which may pose safety concerns for the patient (29). A trial block is therefore not considered best practice for intrathecal analgesic treatment (28).

Medications for intrathecal administration

A variety of medications for somatic, visceral and neuropathic pain; opioids, local anesthetics, N-type calcium channel blockers, alpha-2 agonists (clonidine, adrenaline) and antispasmodics, can be used alone or in combination intrathecally (5). The most commonly used medications include morphine, fentanyl, bupivacaine, ropivacaine and clonidine (5), alongside hydromorphone, sufentanil and ziconotide (1, 12). Clonidine can be added to intrathecal opioids or local anaesthetics to enhance the analgesia and reduce the opioid related side-effects (5), also there is research indicating that bupivacaine acts synergistically with morphine intrathecally (7). Bupivacaine and clonidine appear to be especially beneficial for neuropathic or mixed cancer pain (5). Morphine remains the gold standard (30). Compared to other opioids such as fentanyl or hydromorphone, morphine has a relatively hydrophilic profile thus capable of spreading distal of the injection site and thereby exert effect at multiple spinal levels (31). The Polyanalgesic Consensus Conference 2012 has made recommendations for the management of pain by intrathecal drug delivery (32). As first line drugs for nociceptive pain they recommend morphine, hydromorphone, ziconotide or fentanyl, for neuropathic pain recommendations are morphine or morphine with bupivacaine or ziconotide (32). For second line drugs they are recommending the same opioids in combination with bupivacaine or ziconotide in combination with an opioid. Second line for neuropathic pain includes adding clonidine to first line drugs (32). Deer et al. (16) suggest initiating intrathecal drug delivery at a low rate and slowly titrate to limit the risk of adverse effects. When dose increase is no longer deemed safe with monotherapy, a combination of drugs may be warranted (16).

Many patients with severe nociceptive cancer pain also have a neuropathic component because tissue damage and cancer infiltration affect peripheral nerves (14). Neuropathic pain resulting from major dysfunction of the somatosensory system may not respond satisfactory to opioid therapy, which presents a need to combine opioids with other drugs such as local anaesthetics (14). A double-blind randomised clinical study by Huang et al. found that patients receiving

intrathecal morphine and ropivacaine reported lower pain scores and needed less morphine compared to those receiving intrathecal morphine alone. Negative side-effects were similar in both groups (14).

Breivik (8) claims that administering opioids alone spinally has not shown to be more effective than intravenous or oral opioids in patients with refractory cancer pain. He argues that there is evidence that pain relief can be obtained with a combination of opioids, local anesthetic and an alfa2-agonist. The local anaesthetic is the drug that allows the striking effect, however given alone it would require dosing which would also cause motor-blockade of the legs and total loss of sensation in the lower body. Hence, exploiting the additive analgesic effect between these drugs will allow pain relief whilst minimising side effects (8, 33). Mastenbrook et al. (9) have done a retrospective study which displayed the effect and safety of the combination morphine, bupivacaine and clonidine where all patients obtained freedom from pain after intrathecal treatment was initiated and no serious side effects were observed. Adrenaline can be used as an alfa2-agonist to avoid the sedative and hypotensive effect of clonidine (8).

Adverse effects

Adverse effects may either occur due to the medications or due to the catheter. Opioids are associated with side effects such as respiratory depression, sedation, urinary retention, nausea and vomiting (11, 12, 31). The risk incidence for most of these complications are less frequent with intrathecal administration compared to systemic, but they are still considered to be significant (31). Respiratory depression is potentially the most harmful adverse event, and has even been reported to occur later than 2 hours after administration of intrathecal analgesics (29). If respiratory depression occurs after monotherapy with an opioid, it can be reversed with administration of mixed opioid receptor antagonist (29). The higher up the intrathecal catheter is placed, the greater the risk of respiratory depression (34). Should respiratory deficiency become evident after intrathecal administration of a local anaesthetic, even with supplemental oxygen; assisted ventilation, intubation and mechanical ventilation may be necessary (34). Intrathecal treatment may also cause hypotension due to vasodilatation, sometimes accompanied by bradycardia (34). This should be anticipated and treated rapidly with intravenous fluids, vasopressors and/or move the patient to a head-down position. Bradycardia can be treated with atropine (34). The likelihood of urinary retention is substantial with the use

of local anaesthetics intrathecally in the lumbar level as it may block the sympathetic and parasympathetic control of bladder function (34). Hyperalgesia and tolerance can also occur with long term opioid treatment (29). Catheter related adverse effects can potentially cause serious harm. Catheter tip granulation, bleeding and infection may occur (13, 29) along with fibrosis, cerebrospinal fluid leaks (31) and catheters breaking or kinking (29, 31).

Reduction of systemic opioids after initiation of intrathecal analgesia

Prager et al. (28) maintain that respiratory depression is a key safety factor and potentially the most serious side effect from intrathecal opioids. Hence, they recommend eliminating all systemic opioids when starting intrathecal drug delivery, or if not possible, reduce by at least 50%. Titration of intrathecal opioids should be done cautiously while monitoring for pain reduction and side effects (28).

In a study examined by Mitchell et al. (35) the patients' systemic opioids were converted to short-acting ones and dosing was reduced by 50% four hours preoperatively and again by 50% after initiation of intrathecal drug delivery. Thereafter reduction of the systemic opioids during the next 24-48 hours until the patient only has oral analgesics for breakthrough pain (35). In addition, when converting oral opioid dosing to intrathecal morphine, the dose was reduced by 33% as oral opioid dosing is often high and converting to intrathecal for most patients also means opioid rotation (35). Kim et al. (36) did a retrospective analysis of 22 terminal cancer patients who were started on intrathecal pain management. They found significant lower pain scores 30 days after initiation compared to baseline, although failed to report a significant reduction of systemic opioids in the same time period. This is inconsistent with previous studies that have found significant decreases in systemic opioids (36).

Monitoring of patients with intrathecal catheters

Prager et al. (2014) believe that two of the main therapy-related safety issues concerning intrathecal analgesia are inadequate monitoring and dosing errors (28). They express that all patients should be monitored in a fully equipped and staffed facility for at least 24 hours after start or restart of intrathecal opioid treatment (28). Monitoring should include adequacy of ventilation (respiration rate, depth of respiration), oxygenation (continuous pulse oximetry),

and level consciousness (28). Documentation of vital signs should be done at least every four hours. Naloxone should be easily available, as conversion of dosing from one route to another can be difficult and consequences of inappropriate dosing may be life threatening (28). Prager et al. (28) state that nursing staff need to be educated about the monitoring requirements of patients being treated with intrathecal opioids. Hawley et al. (13) also mention the need of appropriate education for nurses caring for patients with intrathecal infusions, especially in the initiation period (13). McHugh et al. (37) acknowledge that it is vital that nurses caring for patients undergoing interventional procedures understand both the pathophysiology of the disease and the outcome of the intervention. They also agree that initially after the procedure of placing the intrathecal catheter, the patients should be monitored in a recovery or post-anaesthesia care setting. The time required on this level of care depends upon the procedure, the medications used and the patient's status (37). The monitoring of the patients should be done according to the routine of the unit with assessments of ECG, blood pressure, saturation and sedation level in addition to observation of analgesic response, side effects and complications (37). Deer et al. (16) specify that the patients should be carefully monitored for loss of analgesic effect accompanied by new and progressive neurologic symptoms as they are both primary indications of granuloma development.

End of life distress and refractory symptoms

Towards the end of life, some patients will experience so severe pain or other distressful symptoms that they are refractory to most standard treatments. For this group of patients palliative sedation may be the only way to achieve symptom control. The phrase 'refractory' can be used to describe symptoms that cannot be sufficiently controlled despite aggressive efforts to identify a tolerable treatment that does not compromise the patient's consciousness (18, 21, 38-40). To classify a symptom as refractory the clinician must believe that additional interventions are either unable of providing satisfactory relief, associated with increased and unbearable morbidity or unlikely to grant relief within the timeframe available (18, 38-40). The only indication for palliative sedation is management of refractory symptoms (21, 40). All dimensions of end of life distress; physical, psychological, social, emotional and existential, must be addressed in palliative care. The physical symptoms that are most inclined to be refractory are delirium, dyspnea, pain and emesis (21, 40).

Palliative sedation

There is a variety of definitions of what palliative sedation entails, but the general goal is to reduce the patient's level of consciousness to decrease his perception of physical and/or emotional distress. It is used as a last option in managing refractory symptoms (19, 23, 24, 38, 39, 41-43). Palliative sedation can vary in terms of drugs used, depth of sedation as well as continuity and speed of implementation (21, 39). Benitez-Rosario and Morita (44) have tried to establish consensus on when to perform palliative sedation and appropriate sedation levels through a Delphi study with experts from all continents. All the respondent agreed the use of sedatives in cases of refractory delirium and dyspnea secondary to lung cancer (44). Responses about types and levels of sedation did not achieve consensus in any cases Benitez-Rosario and Morita (44) have tried to establish consensus on when to perform palliative sedation and appropriate sedation levels through a Delphi study with experts from all continents. All the respondent agreed the use of sedatives in cases of refractory delirium and dyspnea secondary to lung cancer (44). Responses about types and levels of sedation did not achieve consensus in any cases (44).

Sedatives given in low or moderate doses for symptom control is not classified as palliative sedation. Some literature suggests that limited experience in managing difficult end-of-life symptoms might increase the prevalence of palliative sedation. Maltoni et al. (21) argue that before initiating palliative sedation, a palliative care specialist should be involved in the decision to ensure all other options have been explored.

Bodnar (19) reports that literature which addresses which medications to use for palliative sedation is very limited. Benzodiazepines, barbiturates and propofol are agents used for palliative sedations, some providers also use opioids and psychotropic medications to take advantage of the sedative side effects (19).

Covarrubias-Gomes et al. (38) notes that it can sometimes be very difficult to give appropriate sedation to the terminally ill patients with severe agitated delirium. There has been documented that short acting benzodiazepines like midazolam may worsen delirium and not give adequate sedation in some cases (38). Some authors suggest that propofol is a good and safe choice in these situations in specialised palliative inpatient units for adults. Propofol could be the agent

which allows an agitated patient to be comfortable in the last days of life when benzodiazepines fail to relieve distress (38).

Propofol

Propofol, an anaesthetic agent, is specifically indicated for sedation and anaesthesia. It has a very rapid time of onset and peak effect and no ceiling to CNS depression (19). The European Society of Medical Oncology's (ESMO) guidelines for the management of refractory symptoms at the end of life presents propofol as an option for palliative sedation (38). It has proven to be useful in patients who has developed high levels of tolerance to benzodiazepines (38). Since its introduction to clinical practice in 1986, propofol has been used during anaesthesia in surgical procedures, as a sedative for non-invasive procedures, but also to control other conditions such as chemotherapy-induced emesis and status epilepticus (38). Propofol rapidly induces unconsciousness and may consequently be an effective option when standard medications for palliative sedation have failed (25). It is administered intravenously, as a continuous infusion for palliative sedation, and is easily adjustable due to its rapid time of onset and short half-life (19). However, what is published on the use of propofol in this setting is anecdotal (45). Much of the recommended dosing for propofol is based upon otherwise healthy patients undergoing short procedures or surgery (19). Dosing for palliative sedation can be very different. The pharmacokinetics and pharmacodynamics of propofol can differ significantly in critically ill patients on continuous infusions compared to healthy individuals receiving boluses or short-term infusions (19). There have only been a few published cases with the use of propofol for palliative sedation. Of the different sedating agents used for palliative sedation, propofol is clearly the agent most likely to provide reliable relief in the shortest time, however it may not be a choice of many providers as they do not have the appropriate staff or facilities to safely administer this anaesthetic (19). Propofol has a profound respiratory depressant effect and inhibits normal response to hypercarbia which can occur even when used in lower doses, as well as a hypotensive impact (46). A few published guidelines on palliative sedation include propofol among possible sedating agents, mostly as a drug of last resort (23).

Incidence of palliative sedation with propofol

The incidence of palliative sedation found in recent studies varies greatly, ranging from 0-64% (39). Maltoni et al. (2013) explain that the large variety may be due to different care settings,

the incidence is found higher in inpatient care than in homecare (39). In Papavasiliou et al.'s (26) retrospective study comparing characteristics of end-of-life sedations, it was found that propofol was only used for this purpose by medical specialists, none of the general practitioners reported using propofol. It has also been argued that the degree of adherence to palliative care guidelines may contribute to the large differences (39). Also, some studies have been conducted in specialised palliative care units whereas others have focused on physicians with little or no training in palliative care and sedation (39). Several authors propose that propofol should be considered for palliative sedation when standard treatment has failed (25, 38).

There has only been a very small number of published cases with the use of propofol for palliative sedation, representing only about 4% of all published cases. Nonetheless, Bodnar (19) upholds that it has been used in this setting a number of times in unpublished cases. In a survey from 1998 only one out of 96 patients receiving terminal sedation were given propofol (47) whereas in an Austrian survey conducted 2012-2013, propofol was being used in 3% of all palliative sedations (25). Trends from Belgium shows an increase in the use of propofol for palliative sedation, from 11% in 2007 to 23,1% in 2013 (48).

Monitoring of patients under palliative sedation with propofol

Palliative sedation guidelines endorse close surveillance of patients with regards to symptoms and suffering, level of consciousness and potential adverse events of sedation (21). Still, monitoring of patients under palliative sedation for symptom control is an area where research is hardly excitant (49). Most guidelines recommend assessment every 15-30 minutes the first hour or two, then 2-3 times daily thereafter (23). Adverse effects are typically seen with rapid injections, large doses and old age. Studies that specifically address respiratory and hemodynamic depression are mainly done on doses used for induction of general anaesthesia (19). Several authors suggest that propofol should be titrated until satisfactory symptom relief without unacceptable adverse effect is achieved (38, 50, 51). The caregiver should remain with the patient until safe and effective dose is found (38, 50, 51). Further they recommend that the patient should be closely monitored the first hour of treatment, with assessment of symptom relief and level of sedation (38, 50, 51). When satisfactory symptom relief is reached, monitoring should take place after 2, 6 and 12 hours. Thereafter, evaluation of effect and sedation level should take place at least twice daily. If the patient is showing signs of drug

induced respiratory depression, infusion should be stopped for 2 or 3 minutes then restarted at a lower rate (38, 50, 51). Analgesics should be continued, as propofol does not provide pain relief (38, 50, 51). Other authors advise that the health care team should establish the suitable intervals for assessing the effect of palliative sedation (49).

There are different views with regards to the value of monitoring vital signs under palliative sedation, although it is found important under sedation in other settings. Some authors claim it would represent a burden for the patient (52). Levy and Cohen (40) recommend that vital signs should be monitored at the start of treatment for the reason of searching for signs of reduced distress, such as decrease of blood pressure, respiratory rate and pulse. They write that once suitable sedation has been accomplished, routine monitoring of vital signs should be discontinued so that the patient does not get disturbed unnecessarily (40). The ESMO Guidelines Working Group (18) recommend no routine monitoring of vital signs in the imminently dying. They write that respiratory rate is primarily monitored to ensure that respiratory distress and tachypnoea are not present (18, 45). If life threatening respiratory depression occurs, a lower dose may be required (18). Although acknowledging that evidence based specific best practise recommendations have yet not been developed, the ESMO guidelines working group advocates the importance of procedural guidelines on institutional level so that the clinicians have a framework for decision making (18).

Cherny (45) suggests that type of patient monitoring should be determined by the goal of care. When the goal of care is to 'ensure comfort until death for an imminently dying', the only parameters for on-going observation are those pertaining to comfort. Heart rate, blood pressure and temperature do not contribute to this goal of care and can be discontinued (45).

Qualification requirements for those attending to patients under palliative sedation with propofol

Maltoni et al. (39) advocate that palliative sedation requires a multi professional clinical approach. Nurses with experience in giving palliative sedation have identified knowledge, skills and guidelines as important aspects to achieve correct implementation of palliative sedation (39). Bodnar (19) advise that prescribers and nurses attending to patients receiving palliative sedation with propofol should be intimately aware of this anaesthetics pharmacokinetics and

pharmacodynamics to effectively and safely dose and administer. Administering propofol requires appropriately trained and experienced staff as it may require frequent adjustments, has a very short time for effect and recovery, and has potential to cause both hypotension and respiratory depression (19, 46). It has been argued that ideally administration of propofol should be done under the supervision of an anaesthesiologist (53).

Wolf (54) presents in his article that it could be justifiable to consider a nurse anesthetist to be involved in the administration of palliative sedation, although this has not been discussed in any other literature found. He claims that a nurse anesthetist can provide theory-based nursing care coupled with speciality education and training in pharmacology and physiology, that would make them suited for assessing, diagnosing, implementing and evaluating palliative sedation (54). Other authors describes nurses working at wards as the ones attending to patients under palliative sedation with propofol (55). The guidelines reviewed by Schildmann et al. (23) recommend sedations with propofol are only performed by an experienced practitioner, but are otherwise very unspecific with regards to who should monitor the patient under sedation and what qualification or education they should behold.

Norwegian standard for anaesthesia (56), an agreement between The Norwegian Society of Anaesthesiologists and the Norwegian Society of Nurse Anesthetists, petitions that sedation with intravenously administered anaesthetic drugs should only be conducted by anaesthetic personnel. The monitoring required will depend upon the patient's health status and the plan for sedation depth, but oxygen saturation should always be monitored (56). An anaesthesiologist should always be available. All personnel administering sedatives must have the knowledge of recognising and treating potential adverse effects, including bag-ventilation and CPR (56). Equipment for treating complications should always be present when sedations are conducted (56). This agreement is composed for anaesthesia in a surgical setting and may not be intended as guidance for palliative sedations.

MATERIAL AND METHODS

Research design and variables

This master thesis is structured as a descriptive cross-sectional survey in the use of intrathecal analgesia and palliative sedation with propofol in Norwegian palliative care units, with a comparison to documentation found in international scientific research literature. The research questions are listed in the background chapter and a detailed list of questions and variables is attached (attachment 3). For each research question the most commonly used routines in the Norwegian palliative care units for these treatment modalities are displayed and compared to the documentation found in the literature. A comprehensive search in scientific databases was carried out to establish solid grounds for comparison between local practice and research literature. All the research literature is presented in the background chapter, thus justifying this chapter being slightly extended.

Approach for the search process and review of the literature

Searches for literature where made in the PubMed, Medline, Cohrane, Embase, Svemed+ and Cinahl databases. The reference lists for the guidelines/recommendations at UpToDate were also investigated. Search words/phrases and combination of these are specified in attachment 1. About 50 articles on intrathecal analgesia and 40 on palliative sedation with propofol were reviewed. Some articles were found from reference lists and suggestions of similar articles in PubMed.

Articles published in Norwegian, Swedish, Danish or English were included in the literature search. Articles from all countries were seen relevant, although it is possible that in regard to palliative sedation it may be differences between countries allowing euthanasia and those who do not. Literature relating to children, adolescents and animals were excluded. The articles have been reviewed and analysed in the light of the research questions for this master thesis.

Source evaluation

Checklists was used in the process of evaluating the literature, then it was structured in a table with main points (see example below). All the articles used have been published in journals

with per-review and all the authors have claimed they have no conflict of interest. One review article by Bruel and Burton has been partially funded by a Jazz Pharmaceuticals, otherwise none of the other studies have been funded by pharmaceutical companies. Most of the literature on palliative sedation with propofol used in this thesis are reviews or case studies. There are few interventional or randomised trials. Presumably this is due to the nature of this treatment modality and the rarity of those in need of this. It would possibly even be ethically questionable to carry out randomised trials in the population of patients in need of palliative sedation. The ESMO Guidelines Working Group (18) and Schildmann et al. (23) also recognise that good quality evidence on management of refractory symptoms at the end of life is absent, and current recommendations should only be looked upon as expert opinions.

Example of literature table:

Authors, title, journal, year	Aim	Method	Result	Comments
Prager, J. Deer, T. Levy, R. Bruel, B. Buscher, E. Caraway, D. *Best Practices for Intrathecal Drug Delivery for Pain* Neuromodulation Journal 2013	To identify best practices and provide guidance to clinicians to ensure safety optimise intrathecal drug delivery for chronic intractable pain.	Twelve experienced pain medicine practitioners (different specialities) from the US, Australia and Europe gathered to identify and publish consensus on best practice for three areas related to safe intrathecal therapy for pain: safety and monitoring, patient and device management, patient selection and trialling.	-Respiratory depression main concern -Monitoring in fully equipped and staffed facility in at least 24 hours after initiation -Eliminate systemic opioids or if not possible, reduce by at least 50 %. -titrate opioids cautiously -all patients should have a trial before implantation	Expert opinion guidelines
Maltoni, M. Setola, E. *Palliative Sedation in Patients With Cancer* Cancer control 2015.	To review literature on palliative sedation in various technical, relational, and bioethical perspectives	Literature review.	-Incidence may vary with definition of palliative sedation. -The incidence may be higher if the care provider has limited experience in managing difficult symptoms. -Recommend close surveillance of patients -During titration phase of sedation, clinical parameters should be evaluated every 15 to 30 minutes (depending on drugs used), and after appropriate sedation level reached, assessment every 24 hours.	Palliative sedation in general, not specified on propofol. Studies used had numerous biases, authors concluding that the data are insufficient, and the evidence is of poor quality with regards to qualitative effectiveness of palliative sedation.

The process of data collection for the Norwegian palliative units

Before starting the process of collecting information from the Norwegian hospitals, available information on the websites of the Regional Committee of Ethics (REC) and Norwegian Centre for Research Data (NSD) was checked to be certain it was not necessary to register this project.

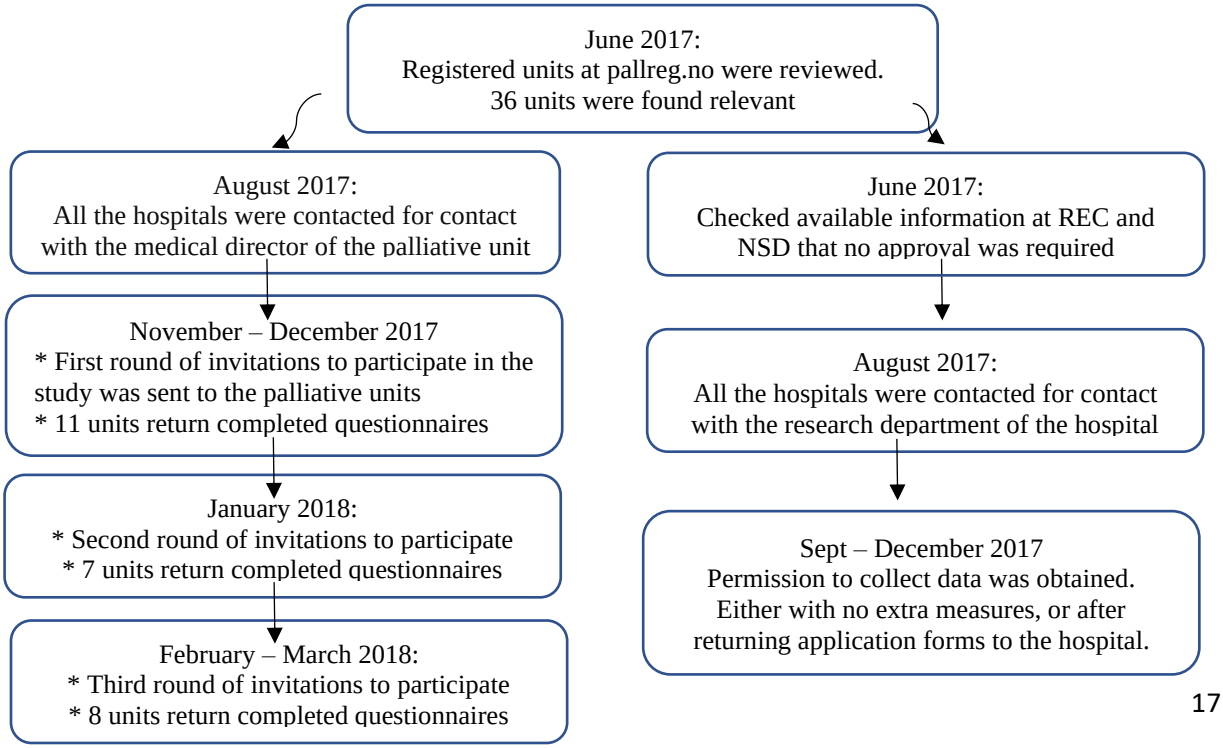
Information about the practice for intrathecal pain treatment and palliative sedation with propofol in Norwegian palliative units was collected through one questionnaire. Palliative units

were identified through the national registry for palliative care units; www.pallreg.no. 36 units were found relevant (only palliative teams or palliative wards, rehabilitating units were not considered relevant), and they were all contacted and asked to contribute in this survey.

The research department at each hospital was contacted to establish the hospitals procedures with regards to collecting data. Some hospitals did not require any further information, and others had specific application forms that needed to be returned. Each hospital's procedure was followed before we retrieved any information from the palliative units.

The invitation to participate was sent by e-mail addressed to the medical director/chief senior consultant, and contained a letter describing the project (attachment 2) along with the questionnaire (attachment 3). The medical directors were asked to either complete the questionnaire themselves or refer to another colleague with better grounds for responding to the questions. The completed questionnaires were returned by e-mail or by post.

After the first invitation to participate, reminders were sent up to two additional times to each unit ensuring as many as possible would participate. In total 26 units returned completed questionnaires between November 2017 and March 2018. The selection of units that has completed the questionnaire represent all health regions in Norway and include both large and small hospitals.



About the data from the units

The questionnaire was designed by the master student and supervisor for this project as there were no validated questionnaires for this purpose available. The questionnaire collects more information than what is needed to cover the research questions. Some of the extra data will be displayed as descriptive analysis at the end of the results chapter to give additional information about the Norwegian practice for the two treatment modalities in question. Also, in addition to this thesis, a research article may be authored, in which other details of the practice would be displayed.

The first part of the questionnaire contains questions about the unit to establish the size and what medical specialities they have available in their teams. Thereafter are questions about intrathecal analgesia which relates to frequency, which other options has been explored (options beyond the WHOs pain ladder), technical details of the insertion and patient safety factors in connection with the start of intrathecal treatment. The last part is questions about the units practice for palliative sedation with propofol, where the questions are aiming to get information about frequency, monitoring and which health care personnel that are involved in this treatment. There are no questions about sedation levels as there is implicit that sedation is given until acceptable symptom relief is obtained, and for this study all levels of sedation were found relevant. The questions are designed to map which monitoring or other patient safety measures the units apply alongside evaluating and adjusting sedation levels. Also, the data collected from the hospitals were only intended to reflect the units' practice and not individual patient data, hence no questions about pain scores or patient satisfaction.

Not all the units have replied to all the questions. Some units have not implanted any intrathecal catheters or performed any palliative sedations with propofol, some units send their patients to larger hospitals for the procedure of implanting the intrathecal catheter and one unit has chosen to use epidural instead of intrathecal pain treatment for this group of patients. These variations lead to the total number of relevant respondents to each question will vary.

Exclusions

Replies relating to specific treatment details from the three units who has not performed any of the treatments in question and also reported having no formal guidelines, has been excluded due to the level of uncertainty connected with these answers. Only information about on-call senior consultants from the units that has an in-patient ward has been included.

Question no: no of answers/ total relevant respondents	**Question no: no of answers/ total relevant respondents**	**Question no: no of answers/ total relevant respondents**
1: 24/26	10a: 23/23	17: 21/23
2: 26/26	10b: 23/23	18: 26/26
3: 26/26	10c: 23/23	19: 26/26
4: 26/26	11: 25/26	20: 26/26
5: 16/16	12a: 23/23	21: 10/10
6: 26/26	12b: 12/14	22: 25/26
7: 26/26	13: 20/23	23: 10/10
8: 26/26	14: 21/23	24: 10/10
9: 26/26	15: 23/23	25: 10/10
	16: 23/23	26: 9/10

The information on how many inhabitants the different units are serving has been compared to information found on the hospitals' official websites. Some hospitals serve the same geographical area, and this has been taken into account when calculation the total population served by these hospitals.

Statistics and presentation of the data

The data from the questionnaire that the units have completed, was organized in an Excel spreadsheet. The data is presented in the results chapter. Mostly the data is presented for all the units as a group, but has been stratified either by region or hospital size for some of the questions. All the answers related to intrathecal or palliative sedation are listed in tables of results (attachment 4).

It has been used descriptive statistics to display the data in this thesis. The data has been described text as well as with mean, median and mode, along with figures and graphs. The data set is small, and a large part of the answers are based on estimates. Statistical testing of probability was not appropriate for this study. Calculation of sample size was not necessary as the total population (all Norwegian palliative units) were invited to participate.

Ethics

The project protocol was reviewed and approved by the Head of department. The study has not compromised patient confidentiality as none of the information collected identifies any specific patient, it solely focuses on hospital practice. The author/master student has no conflict of interest in this study. This study is a quality assurance project of a health service and therefore not required to obtain approval from the Regional Ethics Committee.

The data collected from the palliative care units has been treated with confidentially and made available only to the persons working on this project (master student and supervisor). To ensure the anonymity of the units, the units have been given a random unit number for the presentation of the results, and some of the information about the unit has not been presented in full.

RESULTS

The units

The participating units in this study have reported serving a population of about 4 188 000 (the total Norwegian population currently being approximately 5 300 000 (57)). They include hospitals from all parts of the country and of all sizes. All the larger hospitals are included. The tables below show how the participating units are spread both by region (fig. 2) and by size (fig. 3). Hospitals classified as large in this setting are hospitals serving a population of more than 300 000, mainly university hospitals. Mid-sized hospitals are regional hospitals serving a population of 50 000-300 000. The smaller hospitals are local hospitals serving a population of less than 50 000.

Out of the units participating in this survey, seventeen had an in-patient ward and nine had teams only. Some of the in-patient wards are not administratively a palliative ward, but other medical or oncological wards with a certain number of beds reserved for the palliative units to use (later referred to as *palliative beds*). Six hospitals have palliative wards which is exclusively for palliative patients (later referred to as *palliative ward*). The number of beds at the wards vary from 2 to 12, with the mean being 5,6 (median 4).

Thirteen of the units reported having an anaesthesiologist in the team. Two of the units without an anaesthesiologist employed in the team, reported having close support and regular assistance from an anaesthesiologist working in the anaesthesia department. Seven of the nine units with teams only had an anaesthesiologist in the team.

Out of the seventeen units with in-patient wards, only eight units had a senior consultant with speciality in oncology or palliation on-call 24 hours a day. The other nine units had the on-call shift covered by consultants of other specialities. The spread is shown in fig. 4 below. One unit did not have senior consultants on-call.

54% of the units report having formal guidelines for intrathecal treatment. 38% of the units confirm that they cooperate with the pain management team with regards to intrathecal analgesia and 77% of the units have regular contacts in the anaesthesia department for assistance with intrathecal catheters. Two of the hospitals which do not offer intrathecal treatment in their own unit, refer eligible patients to another hospital for the procedure of implanting the catheter. One unit has chosen to use epidural analgesia instead of intrathecal.

Only five of the units have formal guidelines for palliative sedation with propofol.

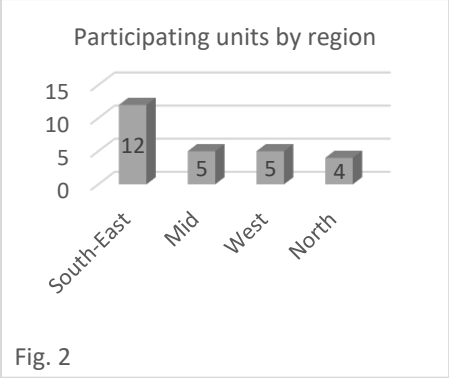


Fig. 2

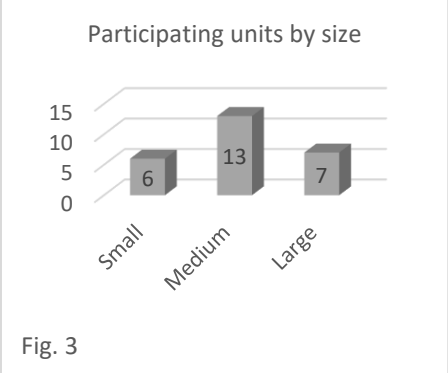


Fig. 3

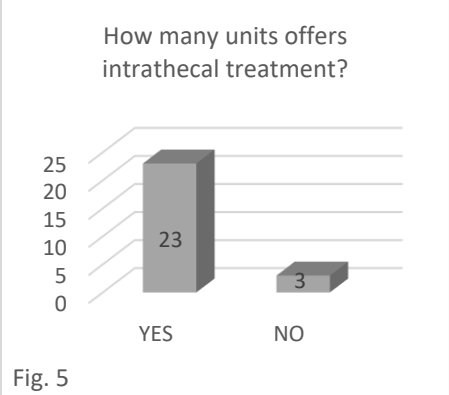


Fig. 5

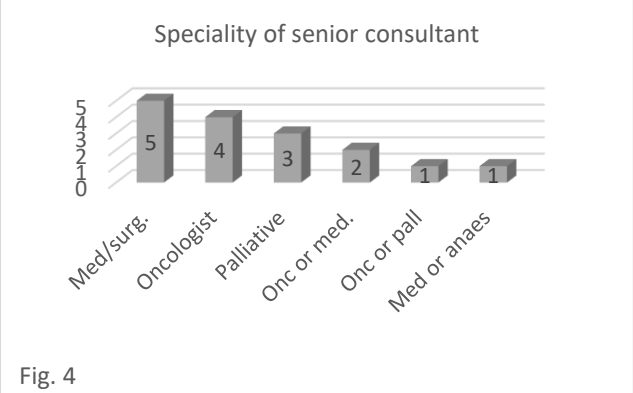


Fig. 4

Intrathecal treatment

Which other analgesic treatments does the unit often try before considering intrathecal analgesia?

The Norwegian palliative units were asked to report which of the following analgesic treatment options they usually try before considering intrathecal analgesia, when standard treatment according to the WHO guidelines fail to provide sufficient pain relief; per os opioid rotation, sub cutaneous opioid infusion, sub cutaneous opioid rotation, intravenous opioid infusion, intravenous opioid rotation and low dose ketamine.

The results show that subcutaneous opioid is usually tried in nearly all the hospitals. Oral opioid rotation is also commonly used in most hospitals. Approximately half of the units usually try subcutaneous opioid rotation and ketamine. Intravenous opioid is a lesser used option, with only six units reporting using this and three units have often tried intravenous opioid rotation. The spread is displayed in figure 6.

Some units have commented that it may vary from patient which options they try. On average the units reported three different treatments which usually are tried before intrathecal analgesia. Smaller hospitals are reporting using more options than the larger ones. The smaller hospitals are reporting an average of 4,5 other analgesic treatments (median and mode 4) whereas the medium hospitals reports an average of 2,9 (median and mode 3) and larger hospitals an average of 2,7 (median 3 and mode 4).

Which medications are most frequently used for intrathecal analgesia?

Fourteen units replied that they use a standard mix of medication for intrathecal pain treatment, whereof one unit had two standard combinations. Seven units reported morphine and bupivacaine as their standard. Five units used a combination of fentanyl, bupivacaine and adrenaline and one unit have morphine, bupivacaine and clonidine as their standard (tab. 1). This shows that all the units are using bupivacaine in combination with an opioid, but the choice of opioid are differentiating the units as well as the ratio between local anaesthetic and opioid and whether or not they are adding an alfa2-agonist.

Nine units did not have a standard mix and two of the fourteen units with a standard medication combination did not know which agents were used.

How is the units' practice for reduction of systematic opioids after initiation of intrathecal analgesia?

Fifteen of the units reduce systematic opioids at the start of intrathecal treatment, whilst five awaits effect of the intrathecal analgesics. One of the units has replied both options. This shows that the practice is divided, with about two thirds (67%) reducing at start and one fourth (24%) await intrathecal response.

If stratifying the data by regions, we find that more than 80% (14 out of 17 units) of the hospitals in the middle and southeast of the country opt to start reducing oral opioids at start of intrathecal treatment, whereas in the units in the north and west only 25% (2 out of 8) are choosing start reduction at start.

How and where are patients being monitored when intrathecal analgesia is initiated?

The procedure for implanting the intrathecal catheter is done in an operating theatre in half of the units, and about a third of the units utilise an intensive care ward for this purpose. Only three units report performing this procedure in the patient's room, two of these are hospitals with palliative wards. One unit has an own treatment room the pain management team uses for these kinds of procedures (fig. 7).

The three units that perform the procedure of implanting the catheter in the patient's room, keeps the patient there for monitoring after the procedure. Another four units send the patients straight to ward after performing the procedure in an operating theatre or treatment room. The most common routine is to transfer the patient to a recovery/intensive care unit for a period of time after the procedure. In ten units the patient will stay at the recovery/intensive care unit for 1-3 hours, in four of the units for 4-12 hours whilst two units report having the patients at this care level for 12-24 hours (fig. 8). These answers are based upon procedures without complications.

When hospitals were stratified according to which type of inpatient ward they had available, some difference can be shown. In the hospitals with palliative wards, the spread is half and half between directly back to the ward and 1-3 hours in recovery/intensive care unit, none of the patients are staying any longer at this level of care. In the hospitals with palliative beds, less than a quarter of the units send their patients straight to ward and time at recovery/intensive care is up to 24 hours.

Titration of intrathecal dosing and changes of intrathecal medications are done by an anaesthesiologist in half of the units, and by a palliative clinician in the other half. One unit reports these changes are done by an intensive care nurse from the pain management team.

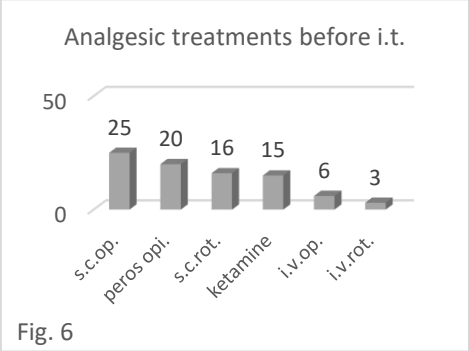


Fig. 6

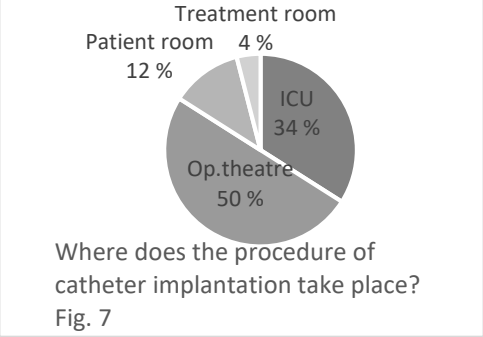


Fig. 7

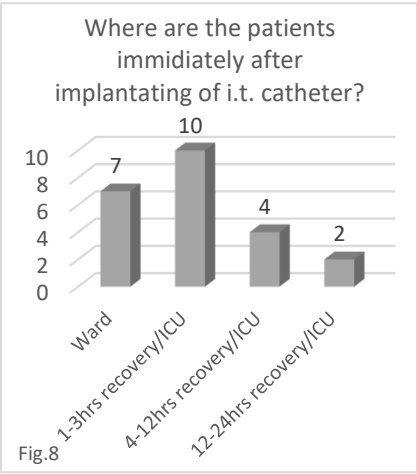


Fig.8

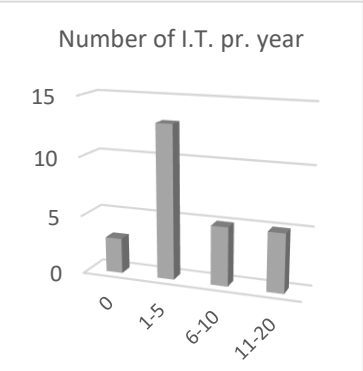


Fig.9 - 73% of the answers are estimates, 27% from register

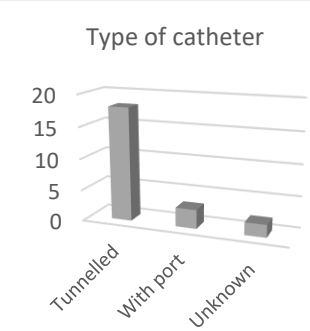


Fig. 10: the incicion is made close to effect site in 60% of the cases

Frequency	Opioid	Local anaesthetic	Alfa2-agonist
4	Morphine 0,25mg/ml	Bupivacaine 0.5mg/ml	
4	Fentanyl 2 mcg/ml	Bupivacaine 1mg/ml	Adrenaline 2 mcg/ml
2	Morphine 0,5mg/ml	Bupivacaine 0,5mg/ml	
1	Morphine 0,5mg/ml	Bupivacaine 0,5mg/ml	Clonidine 5 mcg/ml
1	Fentanyl 2mcg/ml	Bupivacaine 0,5 mg/ml	Adrenaline 1mcg/ml
1	Morphine epidural 0,2mg/ml	Bupivacaine 2,5mg/ml	
2	Unknown		

Tab. 1

Palliative sedation with propofol

What proportion of the palliative units have used propofol for palliative sedation the last two years?

This study reveals that ten units have used palliative sedation with propofol within the last two years, whilst sixteen units have not, meaning just over a third of the palliative units has utilised this treatment modality over the last two years.

Two units have reported just one sedation, five units have reported 2-4 sedations whilst three units have reported 5-7 sedations within the last two year. The highest frequency was 7 sedations for one unit. The collective frequency is also displayed in tab. 2.

If the data is stratified by hospital size (table 2), the frequency for propofol-based sedation in the larger hospitals appears to be nearly doubled compared to the small/medium sized ones.

Where is the patient when palliative sedation with propofol is initiated and which vital parameters are being monitored?

Almost all the units have chosen to carry out palliative sedation with propofol in the patient's room at a palliative or other ward. Only two units have reported that the palliative sedation took place at an intensive care unit, whereof one has disclosed the reason for this being that the patient was already admitted at the intensive care unit prior to the sedation. None of the larger hospitals have used other facilities than the patients room.

The results from the questionnaire show that most units (90%) monitor the patient's respiratory frequency at the beginning of palliative sedation with propofol, and about half of the units monitor the oxygen saturation level, blood pressure and heart rate. Very few reports using ECG or other monitoring. (fig. 11)

For the continuation of the sedation, most units report less monitoring of the patient's vital parameters. Four of the ten units still monitor respiration frequency and three units monitor

oxygen saturation. At this stage monitoring is no longer continuously, but carried out as controls a few times daily (fig.12).

Which health care professionals are responsible for titration and monitoring of patients under palliative sedation with propofol?

The data shows that an anaesthesiologist, either from the palliative team or working in the anaesthesia/intensive care, almost exclusively is responsible for initiation of palliative sedation with propofol. Only one unit has replied clinician from other speciality, and one unit reported a shared responsibility between anaesthesiologist and intensive care nurse. However, for ongoing sedations, health care staff from several specialities are involved. There is still a dominance of anaesthesiologists, although here the results show that doctors and nurses from palliative wards are also represented. Intensive care nurses, and doctor/nurse at other wards are used to a lesser degree. The spread of personnel involved are shown in fig. 13.

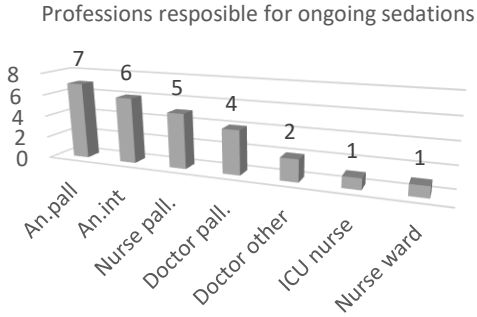


Fig. 13

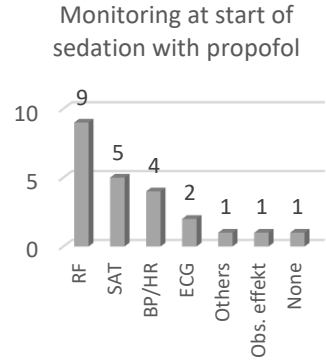


Fig. 11

Unit size	Serving a population of	No. of sedations with propofol over 24 months	Yearly frequency
Large (>300 000 per unit)	2 060 000	21	1 per 196 190
Small/medium (≤300 000)	2 128 000	11,5	1 per 370 087
Total	4 188 000	32,5	1 per 257 723

Table 2

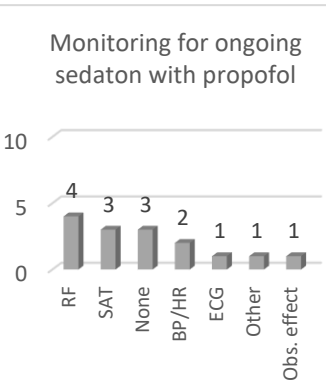


Fig. 12

DISCUSSION

Which analgesic treatments have been tried before intrathecal therapy?

The findings show that nearly all the hospitals try subcutaneous opioid infusion and oral opioid rotation before exploring the option of intrathecal treatment, and about half of the units also report trying subcutaneous opioid rotation and ketamine infusion. Other options are lesser used.

The review of the international research literature shows that most authors highlight that an optimal trial of the WHO's pain ladder for treating cancer pain must be carried out before moving to intrathecal treatment (5, 16). Apart from this, documentation on which treatment options that should be explored when an optimal trial of the ladder fails to provide relief seems almost non-existent. The WHO's pain ladder is based on 'by the mouth' and 'by the clock' as a standard. The ladder does not specify treatment pathways such as sub cutaneous or intravenous (58). It may be argued that per os opioid rotation is part of an optimal trial of the WHO's ladder, but thereafter options are chosen by clinical judgement. In the Norwegian units it appears to be a consensus to try subcutaneous opioid infusion before moving to intrathecal.

Findings from this study also reveal that some hospitals try only one option before moving to intrathecal, whereas others have listed as many as six. Although it is unlikely that all six options are used on all patients, it appears that the smaller hospitals utilise a wider repertoire of these less invasive treatment options before moving to intrathecal. Is this an indication that the units which have reported just the one option are moving too quickly to intrathecal, or are those who try several options putting the patient through unnecessary distress? The difference in how many analgesic treatment options that are tried before moving to intrathecal, may possibly suggest that the smaller hospitals have less accessibility to anaesthesia resources and specialised team members. Should the hospitals where the procedure of implanting intrathecal catheter is not performed, refer their patients to another hospital sooner? On the other hand, perhaps it would be warranted to try more of the less interventional treatments, because moving to another hospital further away from home would represent an additional burden to the patient.

Which medications are commonly used for intrathecal delivery?

Half of the Norwegian palliative units report having a standard medication mix for intrathecal analgesia. They are all using an opioid in combination with a local anaesthetic, but differences are seen with regards to choice of opioid, ratio between local anaesthetic and opioid, and whether or not they are also adding an alfa2-agonist.

The literature review shows that there is a variety of medications that can be delivered intrathecally, but the recommendations on choice of medications are largely based upon expert opinions. The opioids used in the Norwegian palliative units are morphine and fentanyl, which is in thread with recommendations from the The Polyanalgesic Consensus Conference 2012 with regards to choice of first line medications for nociceptive pain (32). However, bupivacaine is listed as a first line drug only for neuropathic pain, for nociceptive they recommend it as a line two medication (32). Does this mean the Norwegian units find that most of the patients requiring intrathecal analgesia have a neuropathic component in their pain? It would be reasonable to assume that refractory pain in advanced stage cancer patients would to some extent be deriving from nerves being affected by tumour masses or radiation. Furthermore The Polyanalgesic Consensus Conference 2012 lists clonidine as a line two drug for neuropathic pain and a line three for nociceptive pain (32).

In Deer et al.'s (16) consensus-based guidelines the recommendation is initiating intrathecal treatment slowly with monotherapy, continuing to a combination of drugs only when increasing monotherapy no longer is deemed safe. Other authors, like Breivik (8), argues that monotherapy is not effective enough or will require dosing that will give unacceptable side effects. It may appear that the Norwegian anaesthesiologists are more in agreement with Breivik's (8) arguments as all units have chosen to use a combination of medications instead of monotherapy. Tay et al. (7) also report that there is evidence to support that bupivacaine acts synergistically with opioids. Mastenbroek et al. (9) documented effect from the combination of a local anaesthetic, opioid and alfa2-agonist. Using a combination of drugs that all work on the same process, though via different mechanisms, is likely to cause additive effect and thereby increase the possibility of achieving pain reduction without unacceptable side effects (8).

The literature found provides little arguments as to why one opioid should be better than another. Morphine is the opioid that has been used the most and is more hydrophilic than other opioids thus being able to work on several segments in the spinal cord, however fentanyl is more concentrated and smaller amounts are required (31). This could be part of an explanation for the variances in the Norwegian units. Nor does the literature provide arguments as to why bupivacaine is the first choice of local anesthetic, neither a lot on whether an alfa2-agonist should be added. This lack of consistent guidelines may explain the large variances in ratio between local anaesthetics and opioids, as well as inconsistency with regards to exploiting an alfa2-agonist, which are found in the Norwegian units.

None of the Norwegian units has reported using Ziconitide (Prialt) although this N-type calcium channel blocker is widely mentioned in the international literature on intrathecal pain treatment. Perhaps this is due to unfamiliarity with this agent, or it may be also question of cost or other factors.

When to reduce systemic opioids

Another side of intrathecal treatment which is lacking clear guidelines is when to reduce systemic opioids. The results show that the majority of the Norwegian units start reducing the patients systemic opioids at the start of intrathecal treatment, whereas about 20% awaits response from the intrathecal treatment before reducing other opioids. The data may indicate that there are geographical variances in this practice. Variances with regards to this part of the treatment are also displayed in the research literature.

Prager et al. (28) highlight in their article the risk of respiratory depression and consequently recommend that all systemic opioids are eliminated when initiating intrathecal therapy, other authors are portraying methods of converting systemic opioids to short-acting opioids hours before intrathecal therapy is initiated whilst at the same time starting the process of reducing these (35). Yet Kim et al. (36) could not find significant reduction of systematic opioids within 30 days of intrathecal treatment in their study. Diversities with regards to when to reduce systemic opioids may also reflect the multifactorial nature of this patient group. The patients may have pain from areas in the body which will not be covered by the intrathecal, thus will still require systemic opioids. Bruel and Burton (29) also raises the point of keeping some

systemic opioids due to dependency and withdrawal symptoms in case a disruption of the intrathecal delivery should occur and lead to a sudden discontinuation of opioids. However, these factors may be a reason for not completely eliminating all systematic opioids at start like Prager et al. (28) suggest, but should not hinder a partial reduction of systematic opioids.

The lack of evidence based guidelines as to when systemic opioids should be reduced, leaves room for judgement. What would be arguments for reducing at start or waiting for response? Two important factors that must be weighed up against each other would be the risk of opioid induced respiratory depression and satisfactory pain relief. The clinicians are responsible to administer a safe treatment and show caution with regards to adverse effects of opioids, which would endorse reducing systemic opioids at start intrathecal treatment. On the other hand, this interventional treatment is being performed because the patient is experiencing unacceptable levels of pain, and one could argue that reducing the systemic opioids before effect from the intrathecal is in place, would lead to additional distress for the patient and possibly even be unethical. Perhaps this dilemma would favour keeping the patient at a recovery or intensive care unit overnight rather than at a ward, as this could possibly warrant more aggressive dosing of analgesics and a little more hesitancy in reducing the systemic opioids. The data may indicate that there are geographical differences as well when it comes to time for reduction of systemic opioids, which would possibly suggest that local traditions may play a role in decision making as well.

Monitoring of patients when intrathecal therapy is initiated

There are variances in how the procedure of initiating intrathecal treatment is carried out in the Norwegian units. The majority choose the operating theatre for implanting the catheter, some hospitals choose an intensive care room while some units choose to use the patient's room for this procedure. Further differences are also seen in where the patient is observed immediately after the procedure; most commonly the patient has a recovery period in a recovery or intensive care unit. The length of stay at this care level varies from 3–24 hours. About a third of the hospitals elect no time at a higher care level, but choose to monitor the patient in his room at the ward. How and where patients should be monitored when initiating intrathecal therapy are very sparingly documented in the international research literature. This could possibly explain some of the differences in practice between the Norwegian hospitals.

Some authors write that patients should be monitored in a fully equipped and staffed facility (28), though without clarifying which equipment and staff this would entail. Prager et al. (28) recommend that initially after the procedure of placing the catheter, the patient should be monitored in a recovery or postoperative care setting for at least 24 hours. McHugh et al. (37) claim time required at this care level will vary from case to case. The literature found does not specify any discharge criterias before moving the patient back to ward.

It would be reasonable to assume that both an operating theatre and an intensive care unit, possibly also a recovery unit, would qualify as 'fully equipped'. They will have equipment for continuous monitoring of vital signs and ventilation aids, as well as staff familiar with the use of these, so the Norwegian units utilising these options would be in line with Prager's recommendations. It is however more questionable as to whether 'fully equipped' would apply for the patient's room. The procedure is done by an anaesthesiologist, but how long he/she will stay with the patient after the catheter is in place is unknown. After the anaesthesiologist leaves, the patient will be monitored and cared for by the personnel at the ward. Typically, nurses at wards will have the responsibility for care of several patients and thus not able to continuously stay in the patient's room. The level of education, experience and training the nurse have for this specific procedure may possibly influence the nurse's response and judgement with regards to the patient's vital signs. Both Hawley (13) and Prager et al. (28) acknowledge that it is vital that nurses caring for patients undergoing interventional procedures have knowledge of the disease and the intervention to safely care for this group of patients. It can be speculated that possible challenges that can occur when initiating intrathecal analgesia at a ward may be equipment and staffing to handle an acute respiratory arrest. In addition, the patient may initially experience vasodilation to the extent that he will require vasopressors to maintain an acceptable blood pressure. Vasopressors for intravenous administration are usually not available at general wards. However, it is possible that the units that choose to use the patient's room for this procedure has ensured extra equipment and medication especially for this procedure, and conceivably also arranged for an anaesthesiologist to be easily available the first 24 hours.

It is possible that the speciality of the resident on-call may be affecting the length of the patient's stay in the recovery unit. The results from the Norwegian units display that the hospitals with more access to senior consultants working only with palliation or oncology, use the recovery unit to a lesser degree than the smaller hospitals where the on-call senior consultant most often

is a specialist in internal medicine or general surgery. The same situation is seen for palliative wards contra palliative beds. Presumably the staff at palliative wards are more experienced in caring for patients with advanced stage cancer undergoing interventional procedures, and therefore more confident in accepting them back earlier from the recovery unit, whereas at a general ward the staff may not be familiar with this intervention at all.

Along with most available equipment, it could be claimed that an operating theatre would provide best environment for initiation of intrathecal treatment also for the reason of avoiding an infection, which can be a catheter related adverse effect (13, 29). This may have influenced the decision in those hospitals that opted to use the operating theatre. Reasons against utilising the operating theatre, may be uncertainties as to when the procedure can be done as it would mean competing for an available time with other surgical activity.

Is palliative sedation with propofol used in Norwegian palliative units?

Palliative sedation with propofol has taken place in about a third of the Norwegian units within the last two years. It is a rare treatment as no unit has reported more than seven sedations. The data may indicate a higher frequency in the larger hospitals, though there are uncertainties relating to this as the total incidence for this treatment is so low and most hospitals have reported estimate-based data.

Palliative sedation can vary by medications used, depth and length of the sedation. Different criterias as to what palliative sedation entails result in large varieties in incidence. The Norwegian understanding of palliative sedation does not include anxiolytics and sedatives given in low or moderate doses. Care setting as well as legal, cultural and organisational factors also contribute to variations in incidence rates (59). The review of literature for this thesis has found incidence rates between 0 and 64% (39), but sedation with propofol would only be a small part of this. These data are from studies done in several European countries, although none from Scandinavian countries. In the limited evidence available on palliative sedations, propofol is regarded as a medication of last resort. If standard medications have failed, propofol should be considered for palliative sedation (23, 38). The low number of palliative sedations with propofol in Norwegian units suggests that propofol is in fact only used as a last resort.

If the larger hospitals are performing propofol based sedations more often than the smaller ones, as the data may suggest, it could be due to larger access to senior consultants in palliative care and anaesthesiologist in palliative teams, as well as palliative wards rather than beds. Patients with the most challenging intractable symptoms would often be transferred from a smaller unit to a larger hospital with a specialised palliative ward. Thus, will patient selection also influence the incidence rates for palliative sedation. Deer et al. (26) describes that care setting and who the patient's care giver is, affects the incidence of palliative sedations.

The data shows that while a few hospitals have executed up to seven sedations in two years, many units report none or just one. Is this number too low? Palliative sedation with propofol is an advanced anaesthesiologic treatment, sometimes the only way to relieve distress, for a small group of patients with intractable symptoms towards the last hours or days of their life. It seems natural to assume that those units where several members of the team and wards are familiar with propofol, would find it easier to use than in those units where very few or none of the staff have experience with using this sedating agent. Perhaps one should argue that the smaller and medium sized hospitals should work towards heightening their experience with this sedating agent so that they also can offer this to eligible patients? Propofol is probably the fastest acting sedating agent used in this setting, and can be able to provide adequate sedation in a short time (19, 25). Nevertheless, the safety aspect of this agent should not be taken lightly, as adverse effects may present themselves just as quickly, and appropriately qualified staff is a necessity. Perhaps the better solution would be for the smaller units to have procedures for transferal of patients to a larger hospital when adequate symptom control cannot be obtained by standard regimens?

Assessment and monitoring of patients under palliative sedation with propofol

The findings show that most units perform palliative sedation with propofol in the patient's room, it seldom takes place in an intensive care unit. Some diversities are found with regards to monitoring. All units monitor respiration frequency at start of sedation, and about half continue to do so during the sedation. Half of the units also report monitoring oxygen saturation, blood pressure and heart rate at start, less continue these measurements under ongoing sedation. Monitoring of other vital signs are uncommon.

Maltoni et al. (21) write in their article that guidelines on palliative sedation endorse close surveillance with regards to symptoms, symptom relief and side effects. Still, research on this is hardly existent DeGraff et al. confirm (49). From the literature review we find that most guidelines recommend assessments of vital signs every 15-30 minutes in the beginning, then 2-3 times daily thereafter, but there is little or no specification as to which monitoring or how it should be done. Norwegian Standard for Anaesthesia states that oxygen saturation should be present at all times under sedations (56), though these recommendations are first and foremost created for sedations in surgical setting. Some may claim that the setting of the imminently dying necessitates different actions than for those in need of a temporary procedural sedation, which could be the reason why only half of the Norwegian units include monitoring of oxygen saturation at the start of sedation. Monitoring of respiration frequency can be done without any equipment, more in thread with the minimally invasive palliative care philosophy. Some describe monitoring as a burden for the patient in this setting (52). It has been mentioned from one of the Norwegian units that monitoring of oxygen saturation in this setting is unnecessary as treatment with oxygen would not be applied. Ventilation would only be supported by a chin lift if airways should become obstructed, or a lower dose of propofol if respiratory rate becomes very low. However, whilst opioids often reduce the patients respiration frequency, propofol may instead reduce ventilation depth. Ventilation depth can be difficult to assess, probably justifying the necessity of monitoring oxygen saturation in addition to respiration frequency, to offer a better picture of the patient's ventilation. Still, there are studies confirming that palliative sedation does not hasten death (18), possibly supporting that sedation with little or no monitoring is the correct clinical judgement. Nevertheless, these studies may not have included sedation with propofol, which has a highly respiratory depressant effect as well as a profound hypotensive impact that may warrant higher levels om monitoring than other sedating agents.

Health care workers involved with palliative sedations

In the Norwegian units it is almost exclusively an anaesthesiologist who is responsible for titration and assessment at the start of the sedation. For ongoing sedations, the responsibility most commonly still lays with the anaesthesiologist, although some units also utilise a doctor or nurse at the palliative ward at this stage of the sedation.

From the literature review we find that documentation on which health care personnel or what qualification they should hold is almost non-existent, although Bodnar (19) argues that those

attending to patients receiving continuous propofol infusions should have profound knowledge of propofol's pharmacokinetics and pharmacodynamics, and have appropriate training and experience. Ideally an anaesthesiologist should supervise it. The data from the Norwegian units does not specify how often or for how long the anaesthesiologist is in immediate proximity to the patient's room, but it is likely to think that it is a nurse working at the ward who is with the patient at all times. Norwegian Standard for Anaesthesia (56) maintain that sedation with intravenously administered anaesthetic drugs should only be conducted by anaesthetic personnel and all personnel administering sedatives must have the knowledge of recognising and treating potential adverse effects, including bag-ventilation. It is worth noting this agreement exists as a base for all sedations in surgical setting to ensure patient safety, however this agreement was not conducted for sedations in palliative setting. Interestingly none of the Norwegian palliative units have reported using a nurse anesthetist for palliative sedations with propofol.

Ethical aspects

This thesis has its focus on procedures and monitoring in connection with advanced treatments for critically ill and dying patients, as patient safety issues are important ethical aspects to these treatments. Intrathecal treatment is an invasive and potent treatment, and could potentially cause harm and consequently extra burden to a patient with advanced disease and short life expectancy. There are obvious ethical quandaries to palliative sedation as reducing someone's level of consciousness, although alleviating them from their distress, also will leave them unable to express themselves and this may be challenging for patient, staff and family. The total loss of autonomy and loss of the ability to experience quality of life, which is a basic value in palliative care, makes palliative sedation ethically challenging (59). Critics has described palliative sedation as "slow euthanasia", yet the intention of palliative sedation is about relieving symptoms and unbearable suffering, not cause premature death (59). It is therefore ethically important that the procedures for this treatment ensures that palliative sedation does not hasten death. In light of this, patient safety aspects such as monitoring and qualifications of those attending to the patient, are also of ethical character.

Another ethical side to this study is whether or not these potent treatments are equally available for patients in all parts of the country. Hospitals which are not able to offer these treatment options in their own establishment would require close cooperation with another hospital.

It has been a premise for this project, that alongside the monitoring and assessment of vital signs which has been reviewed in this thesis, the patient is receiving good and respectful care, with consideration of the physical, psychological and emotional needs.

Strengths and limitations

A strength of this study is that all eligible units in the country were invited and a large proportion of those, 72%, has chosen to participate, contributing to good external validity. Limitations may apply to the internal validity. As the questionnaire has not been validated or used by others, there is an uncertainty as to whether or not the respondents have understood all the questions. Some inconsistencies were found in answers to question 4, suggesting that this question was not clear enough. This has been taken into account when using the data. To collect all relevant information through just one questionnaire is an ambitious task, and some questions have perhaps provided a little less information than sought for. A few more questions about the staff responsible for the patient and which training they are given with regards to handling adverse effects, would have been beneficial. To get more in depth information about each unit's procedures, it could have been useful to carry out a qualitative interview in addition to the questionnaire. On the other hand, this might have resulted in lower participance, as it would have required more time from the units.

Most of the units have responded with estimate data. This can cause some uncertainty about the data. Recall bias may influence some of the answers and reduce the reliability of the questionnaire. There is also a possibility that the answers may have been influenced by the respondents (intentionally or unintentionally) wish to portray their unit in the best possible way. Also, a low number of units in each group, leaves ambiguity when stratifying the data by size or region. This has been done to see if variances or similarities can be found within groups, but it should only be looked upon as possible indications.

Although the questionnaire has not been validated and recall bias may provide some uncertainties, the main findings such as the rarity of the treatment, where the treatments is carried out, most commonly used medications and type of monitoring should still be trustworthy.

The literature on monitoring during palliative sedation is spears, but also none of those found are specific to sedation with propofol, leaving an uncertainty as to whether the recommendations would differ if they were.

Conclusion

The data collected for this master thesis displays that intrathecal analgesia in cancer patients is performed in most Norwegian palliative units. The total number of patients receiving this treatment is low, perhaps indicating that intrathecal analgesic treatment is not accessible to all eligible patients. There is likely that units where the staff, both nurses and doctors, are experienced and confident in attending to patients with intrathecal treatment, would have a lower limit for exploring this option than in units where the staff is unfamiliar with this treatment modality. Diversities between the units are shown with regards to when intrathecal is considered, patient care level in connection with the implantation of the catheter, medications used and when to reduce the systemic opioids. From a patient safety perspective, we find that the clinical judgement of safe practice in connection with initiating intrathecal treatment ranges from performing the procedure of initiating intrathecal treatment in the patient's room whilst awaiting effect before reducing systemic opioids, to reducing at start and keeping the patient closely monitored in an intensive care or recovery unit for up to 24 hours after the procedure. It seems reasonable to argue that in units with a low volume of this procedure and without a palliative ward or palliative specialist on-call all hours, the patient should stay at a recovery or intensive care unit for a period of time after initiation of intrathecal, possibly overnight. Whereas in units with a higher volume of procedures and a palliative ward with palliative specialist on-call, it could be justified to let the patient be monitored and cared for at the palliative ward straight after the procedure, or with just a short time at the recovery unit. In cases where it is considered necessary to await effect of intrathecal before reducing systemic opioids, the patient should stay in the recovery or intensive care unit until appropriate dosing of analgesics is reached.

There is a fair amount of literature that supports the efficacy of intrathecal analgesia for patients with refractory cancer pain, however studies that explore which other treatments should be done before considering intrathecal analgesia are spears. Studies that investigates how and where patients should be monitored when intrathecal treatment is initiated seem non-existent. Kurita

et al. (15) confirms there are few RCTs in this field and the strength of the recommendations thereof is weak.

Palliative sedation with propofol is a treatment option that has taken place in about one third of the Norwegian units within the last two years. The total number of patients who has received this treatment in a Norwegian hospital is very low, which could raise a question as to whether or not it is available to all eligible patients. Variances in the procedures for palliative sedation with propofol between the units are mostly found with regards to monitoring of vital signs during the sedation. Most units choose to perform the palliative sedation in the patient's room, with an anaesthesiologist in charge of titrating the sedation.

The low number of patients receiving both of these treatments, and the variations in how the treatments are being performed, warrant the conclusion that there is a need for further research into both these two treatment modalities to establish evidence-based guidelines to make sure patients receive safe and efficient treatments. The results from this study could suggest that the speciality of the on-call senior consultant and whether or not the unit has a palliative ward influence to what extent the intensive care is used in connection with initiation of intrathecal analgesia and to what extent palliative sedation with propofol is being used. Research into the procedure of implanting the intrathecal catheter and patient safety measures in connection with the initiation, choice of medications, when to reduce systematic opioids and monitoring requirements would be necessary. Further research to clarify safety aspects for palliative sedation with propofol is required to ensure these sedations are carried out safely and without hastening death. Until such evidence is in place, national consensus-based guidelines would be beneficial to secure patient safety and equal access to these potent treatments around the country.

ATTACHEMENT 1: Search history

Intrathecal:

DATO	DATABASE	SØK NR. / SØKEORD	TREFF
5/6-18	PubMed	1: Neoplasms (MESH) (majr)	2 665 468
		2: Cancer	3 690 500
		3: Malign*	525 865
		4: 1 OR 2 OR 3	3 777 743
		5: Palliative	85 825
		6: “end of life”	19 670
		7: Terminal	406 929
		8: 5 OR 6 OR 7	487 842
		9: 4 AND 8	104 244
		10: Intrathecal	20 275
		11: Intraspinal	4 683
		12: Spinal	367 555
		13: 10 OR 11 OR 12	374 818
		14: Analgesi*	565 685
		15: Analget*	2 051
		16: Opioid*	103 598
		17: 14 OR 15 OR 16	601 002
		18: 13 AND 17	26 929
		19: 9 AND 18	414
		Filters: last 10 yrs, english/norwegian/Swedish/Danish, humans, 19+ yrs	61
		20: “interventional management” OR “interventional treatment” OR “interventional therapies”	1 143
		21: pain	738 861
		22: 2 AND 20 AND 21	29
		Filter: last 10 years	19
5/6-18	Medline	1: Neoplasm	3 057 674
		2: Cancer	1 489 202
		3: Malign*	524 111
		4: 1 OR 2 OR 3	3 537 191
		5: Palliative	77 853
		6: “end of life”	93 906
		7: Terminal	407 564
		8: 5 OR 6 OR 7	498 719
		9: 4 AND 8	90 319
		10: Intrathecal	20 305
		11: Intraspinal	4 690
		12: Spinal (infusions, injections, anaesthesia)	26 139
		13: 10 OR 11 OR 12	41 873
		14: Analgesi*	173 444
		15: Analgetic*	2 224
		16: Opioid*	103 716
		17: 14 OR 15 OR 16	224 253
		18: 13 AND 17	10 216
		19: 9 AND 18	174

		Filters: last 10 yrs, humans, 19+ yrs	10
5/6-18	EMBASE	1: Neoplasm	4 123 701
		2: Cancer	3 961 563
		3: Malign*	3 323 680
		4: 1 OR 2 OR 3	4 798 470
		5: Palliative	127 986
		6: “end of life”	28 229
		7: Terminal	551 423
		8: 5 OR 6 OR 7	664 937
		9: 4 AND 8	144 134
		10: Intrathecal (catheter, pump, drug adm.)	19 549
		11: Intraspinal	10 607
		12: Spinal (anaesthesia, dorsal horn)	31 231
		13: 10 OR 11 OR 12	56 771
		14: Analgesi*	282 452
		15: Analgetic*	3 415
		16: Opioid*	105 299
		17: 14 OR 15 OR 16	346 295
		18: 13 AND 17	15 741
		19: 9 AND 18	218
		Filters: 10 yrs, adults, humans	24
5/6-18	SveMed+	1: Neoplasm	8581
		2: Cancer	8701
		3: Malign*	437
		4: 1 OR 2 OR 3	8793
		5: Palliative	1095
		6: “end of life”	96
		7: Terminal	1161
		8: 5 OR 6 OR 7	1753
		9: 4 AND 8	451
		10: Intrathecal	19
		11: Intraspinal	9
		12: Spinal	932
		13: 10 OR 11 OR 12	937
		14: Analgesi*	1389
		15: Analgetic*	16
		16: Opioid*	958
		17: 14 OR 15 OR 16	1684
		18: 13 AND 17	68
		19: 9 AND 18	2
		Filter: last 10 years	0
5/6-18	Cinahl	1: Intrathecal (injections, infusions, catheters)	17 148
		2: Neoplasm	71 292
		3: Pain	244 683
		4: 1 AND 2 AND 3	22
		Filter: last 10 years	11

Palliative sedation with propofol:

DATO	DATABASE	SØK NR. / SØKEORD	TREFF
9/10-17	PubMed	1: «terminal sedation» 2: «terminal care» 3: «hospice care» 4: «end of life» 5: Palliati* 6: 1 OR 2 OR 3 OR 4 OR 5 7: propofol 8: 6 AND 7 9: filter: english/norwegian/swedish/danish (26 articles considered/examined)	158 25216 7138 18193 88467 113704 19606 66 54
11/10-17	Medline	1: «terminal care / palliative care» 2: propofol 3: 1 AND 2 (all of which has been found in PubMed)	91445 13893 25
11/10-17	EMBASE	1: terminal care 2: palliati* 3: hospice care 4: 1 OR 2 OR 3 5: propofol 6: 4 AND 5 7: sedation 8: 6 AND 7 (33 articles considered/examined)	59060 127739 9669 170653 48181 295 80930 157
12/10-17	SveMed+	1: palliative OR palliation 2: propofol 3: 1 AND 2 4: «end of life» OR «palliative sedation» OR «terminal sedation» OR «lindrende sedasjon» 5: 2 AND 4	1070 51 0 142 0

12/10-17: Searched ‘palliative sedation’ on UpToDate -searched reference list

ATTACHEMENT 2: Invitation letter to the Norwegian palliative units

Hei.

Jeg studerer ved NTNU og holder på med en master i klinisk helsevitenskap, studieretning smerte og palliasjon. Som min masteroppgave gjennomfører jeg en kartleggingsstudie av praksis for bruk av smertelindring via intratekalkatetre hos kreftpasienter i palliative fase og bruk av propofol til lindrende sedering ved norske palliative enheter.

Motivasjonen for studien er at til tross for at både vitenskapelig dokumentasjon og klinisk erfaring har vist at intratekalkateter gir god smertelindring, foreligger det lite dokumentasjon både når det gjelder hvilke andre metoder for smertebehandling som bør forsøkes først, hvilke pasienter og hvilke typer kreftsmerter som er egnet for intratekal smertebehandling, hvordan behandlingen bør startes og hvilke medikamentblandinger som bør brukes. I fraværet av dokumentasjon og autoritative retningslinjer vil lokal praksis sannsynligvis variere betydelig, også innad i Norge.

Propofol har i en del år blitt omtalt i forskningslitteraturen som et aktuelt legemiddel ved lindrende sedering, særlig dersom man ikke kommer i mål med benzodiazepiner. Selv om både lærebøker og artikler nevner propofol som et aktuelt alternativ, er det svært begrenset vitenskapelig dokumentasjon for bruk av propofol på denne indikasjonen. Dette både for hva som bør være indikasjoner for bruk av propofol til lindrende sedering og hvordan sedering med propofol skal gjennomføres.

Kartleggingen i denne studien vil både vise omfanget av bruken av disse teknikkene, og dessuten hvilke områder der praksis spriker mest mellom ulike sykehus. Innenfor de områdene der det er stor variasjon i praksis, vil det være særlig stort behov for både forskning og konsensusbaserte retningslinjer.

Målsettingen med denne oppgaven er altså å kartlegge bruken av intratekal smertelindring og propofol til lindrende sedering ved norske sykehus med palliativ avdeling og/eller palliativt team. Aktuelle palliative virksomheter har blitt identifisert via det nasjonale registeret over palliative virksomheter; www.pallreg.no.

Jeg håper du har anledning til å svare på spørsmålene i det vedlagt spørreskjemaet på vegne av din enhet, eventuelt henvise til en annen overlege som har bedre grunnlag for å svare på spørsmålene. Data fra hver enkelt avdeling vil bli behandlet konfidensielt og ikke bli gjort tilgjengelig for andre enn studiemedarbeiderne. Masteroppgaven kan sendes avdelingen i etterkant om ønskelig. Det er en målsetting å publisere resultatene fra studien et internasjonalt tidsskrift med fagfellevurdering.

Hovedveileder for oppgaven er professor/overlege Olav Fredheim ved NTNU og Palliativt senter, AHUS.

Med vennlig hilsen,
Siri Kosberg Morseth
E-post: sirikm@stud.ntnu.no
(mob: 47259911)

ATTACHMENT 3: Questionnaire

SPØRRESKJEMA OM INTRATEKAL SMERTEBEHANDLING OG LINDRENDE SEDERING MED PROPOFOL

OM ENHETEN

1. Pasientgrunnlag (antall) i opptaksområdet _____
2. Palliativ sengepost ____ Antall senger _____ Palliativt team uten egne senger __
3. Spesialist i anestesiologi ansatt i palliativt team/avdeling ja / nei
4. Har enheten døgnkontinuerlig vaktordning for overleger ja / nei
5. Hvis ja; døgnkontinuerlig vaktordning for overleger dekkes av (sett kryss)

   Medisinsk/kirurgisk vakthavende overlege ……..

   (Generell) onkologisk vakthavende overlege ……..

   Overlege innen palliasjon ……

OM INTRATEKAL SMERTEBEHANDLING

6. Samarbeider palliativ sengepost/palliativt team regelmessig med smerteteam om smertelindring inkl. intratekalkateter? Ja / nei

7. Har palliativ sengepost/palliativt team en eller flere faste kontakter i anestesiavdelingen for hjelp med smertekatetre? Ja / nei

8. Omtrentlig antall intratekalkatetre per år:
   0 1-5 6-10 11-20 21-30 31-40 41-50 >50

9. Hva bygger tallet på? Lokalt register_____ overslag_____

10. Vedr. innleggelse av intratekalkateter:

    a) Hvor gjøres prosedyren vanligvis?
    Pasientrommet_____ Behandlingsrom på sengepost/smerteklinikk_____
    Operasjonsstue _____ Postop/intensiv _____

    b) Hvem utfører prosedyren?
    Anestesilege fra palliativ avdeling _____
    Anestesilege fra smerteteam _____
    Annen anestesilege _____

    c) Hvor ligger pasienten vanligvis etter prosedyren (hvis ukomplisert)?

    På sengepost ____
    1-3 timer på overvåkning _____

4-12 timer på overvåkning _____
12-24 timer på overvåkning _____
>1 døgn på overvåkning _____

11. Har avdelingen formelle prosedyrer/retningslinjer for intratekal behandling? Ja / nei

12. a) Bruker avdelingen vanligvis en standardisert medikamentblanding ved oppstart av intratekal smertebehandling? Ja / nei

b) Hvis ja: hva er blandingen? Angi medikamenter og konsentrasjoner

……

……

13. Gjøres innstikk vanligvis nær nivået man ønsker effekt på, eller stikker man lavt og trer kateteret til ønsket nivå?
Stikker nær nivå for effekt____ Stikker lavt og trer kateteret____

14. Hvilken metode for kateter/pumpe benyttes vanligvis:

Ikke-tunnellert kateter_____
Tunnellert kateter _____
Kateter med «injeksjonsport» for tilkobling til pumpe _____
Kateter med implantert pumpe _____

15. Utføres titrering av dose kun av anestesilege, eller også av palliative leger med annen spesialitet

Kun anestesilege _____ Også av andre palliative leger _____

16. Utføres endring av medikamentblanding av anestesilege, eller også av andre palliative leger

Kun anestesilege _____ Også av andre palliative leger _____

17. Reduseres vanligvis fast dose av systemiske opioider ved oppstart av intratekal, eller avventer man effekt av intratekal (redusert smerte) før man reduserer dose av systemiske opioider
Reduserer ved oppstart _____ Avventer effekt før reduksjon _____

18. Hvilke av de følgende behandlingsmodalitetene vil vanligvis være forsøkt før man velger intratekalkateter:

Peroral opioidrotasjon _____
s.c. pumpe med opioid _____
s.c. opioidrotasjon _____
i.v. pumpe med opioid _____

i.v. opioidrotasjon _____
Lavdose infusjon ketamin _____

OM PROPOFOL TIL LINDRENDE SEDERING

19. Har lindrende sedering med propofol funnet sted ved avdelingen de to siste årene?
    Ja / Nei

20. Omtrent hvor mange pasienter har mottatt lindrende sedering med propofol de siste to årene? _____

21. Hvor ble eventuelt sedasjon med propofol startet opp

    Vanlig sengepost_____ Palliativ sengepost_____

    Intensivavdeling (inkl. postop/intermediær/overvåkning) _____

22. Har sykehuset retningslinjer/prosedyrer for bruk av propofol til lindrende sedering? Ja / Nei

23. Hvilket personale stod for dosering (titrering av dose) ved oppstart av lindrende sedering med propofol?
    -Anestesilege fra anestesi/intensivavdeling _____
    -Anestesilege med palliasjon som arbeidsoppgave_____
    -Anestesilege fra smerteteam _____
    -Annen lege med palliasjon som arbeidsoppgave _____
    -Anestesisykepleier _____
    -Intensivsykepleier _____
    -Sykepleier på palliativ sengepost _____
    -Sykepleier på annen sengepost _____
    -Lege på annen sengepost _____

24. Hvilket personale stod for vedlikehold av lindrende sedering med propofol?

    -Anestesilege fra anestesi/intensivavdeling _____
    -Anestesilege med palliasjon som arbeidsoppgave_____
    -Anestesilege fra smerteteam _____
    -Annen lege med palliasjon som arbeidsoppgave _____
    - Anestesisykepleier _____
    -Intensivsykepleier _____
    -Sykepleier på palliativ sengepost _____
    -Sykepleier på annen sengepost _____
    -Lege på sengepost _____

25. Hva slags monitorering ble utført under lindrende sedering med propofol i oppstartsfasen?

- EKG. Kontinuerlig _____ Kontroll noen ganger daglig _____
- BT/p. Kontinuerlig _____ Kontrollmålinger noen ganger daglig _____
- SAT-måling.Kontinuerlig _____ Kontrollmålinger noen ganger daglig _____
- Respirasjonsfrekvens_____
- Ingen av de ovenstående _____
- Andre: _____

26. Hva slags monitorering ble utført under lindrende sedering med propofol i vedlikeholdsfasen?

- EKG. Kontinuerlig _____ Kontroll noen ganger daglig _____
- BT/p. Kontinuerlig _____ Kontrollmålinger noen ganger daglig _____
- SAT-måling.Kontinuerlig _____ Kontrollmålinger noen ganger daglig _____
- Respirasjonsfrekvens_____
- Ingen av de ovenstående _____
- Andre: _____

ATTACHEMENT 4: Tables of results

INTRATHECAL

Question no.:	6	7	8	9	10a	10b	10c	11
Unit 1	Yes	Yes	1-5	Reg.	OR	An.pain-team	1-3	Yes
Unit 2	No	Yes	1-5	Est.	OR	Other an.	12-24	No
Unit 3	No	Yes	1-5	Reg.	ICU	An.pall	4-12	Yes
						An.pain-.team		
						Other an.		
Unit 4	No	No	1-5	Est.	ICU	Other an.	12-24	No
Unit 5	Yes	Yes	11-20	Reg.	OR	An.pall	1-3	Yes
					ICU			
Unit 6	No	Yes	11-20	Est.	OR	An.pall	4-12	Yes
						Other an.		
Unit 7	No	Yes	1-5	Est.	OR	Other an.	1-3	No
Unit 8	No	No	6-10	Reg.	Pat.room	An.pall	Ward	Yes
Unit 9	Yes	Yes	6-10	Reg.	OR	An.pall	Ward	Yes
Unit 10	No	No	1-5	Est.	OR	Other an.	1-3	No
Unit 11	Yes	Yes	11-20	Est.	OR	An.pall	1-3	Yes
						An.pain-team		
Unit 12	No	Yes	0	Est.				No
Unit 13	No	No	6-10	Est.	Pat.room	An.pall	Ward	Yes
Unit 14	Yes	No	6-10	Est.	OR	An.pain-team	1-3	No
Unit 15	Yes	Yes	0	Est.				No
Unit 16	No	No	0	Est.				No
Unit 17	No	Yes	1-5	Est.	OR	Other an.	Ward	No
Unit 18	Yes	Yes	11-20	Reg.	Treatm.room	An.pain-team	Ward	Yes
Unit 19	Yes	Yes	1-5	Reg.	ICU	An.pall	4-12	Yes
Unit 20	No	Yes	1-5	Est.	OR	Other an.	1-3	No
Unit 21	Yes	Yes	11-20	Est.	Pat.room	An.pain-team	Ward	Yes
Unit 22	No	Yes	1-5	Est.	ICU	Other an.	1-3	Yes
Unit 23	No	Yes	1-5	Est.	ICU	Other an.	1-3	
Unit 24	No	Yes	1-5	Est.	ICU	An.pall	4-12	Yes
						Other an.		
Unit 25	No	Yes	1-5	Est.	OR	An.pall	Ward	Yes
						Other an.		
Unit 26	Yes	Yes	6-10	Est.	ICU	An.pain-team	1-3	No
						Other an.		

Question no.:	12a	12b	13	14	15	16	17	18
Unit 1	Yes	Morph + bupi	Close	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
								s.c.op.
								s.c.rot.
Unit 2	No		Close	Tunnelled	Anaest.	Anaest.	Start	p.o.opi.rot

				Port				s.c.op.
								s.c.rot.
								Ketamine
Unit 3	Yes	Morph + bupi + catapr	Close	Tunnelled	Anaest.	Anaest.	Await	p.o.opi.rot
			Low	Port				s.c.op.
								i.v.op.
								i.v.rot.
Unit 4	No		Close	Tunnelled	Anaest.	Anaest.	Await	p.o.opi.rot
								s.c.op.
								s.c.rot.
								Ketamine
Unit 5	Yes	Morph + bupi	Close	Tunnelled	Other pall.	Anaest.	Await	s.c.op.
		Fent + bupi + adr						Ketamine
Unit 6	No		Close	Tunnelled	Other pall.	Other pall.	Start	s.c.op.
								s.c.rot.
								Ketamine
Unit 7	Yes	Unknown	Unknown	Unknown	Anaest.	Anaest.	Unknown	s.c.op.
								s.c.rot.
Unit 8	Yes	Fent + bupi + adr	Close	Tunnelled	Anaest.	Anaest.	Await	p.o.opi.rot
								s.c.op.
								s.c.rot.
								Ketamine
Unit 9	Yes	Morph + bupi	Low	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
								s.c.op.
Unit 10	No		Unknown	Unknown	Anaest.	Anaest.	Unknown	p.o.opi.rot
								s.c.op.
								s.c.rot.
								i.v.op.
								i.v.rot.
								Ketamine
Unit 11	Yes	Morph + bupi	Close	Tunnelled	Anaest.	Anaest.	Start	p.o.opi.rot
				Port				s.c.op.
Unit 12								p.o.opi.rot
								s.c.op.
								s.c.rot.
								Ketamine
Unit 13	Yes	Morph + bupi	Close	Tunnelled	Other pall.	Other pall.	Start	i.v.op.
Unit 14	Yes	Morph + bupi	Close	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
								s.c.op.
								s.c.rot.
Unit 15								p.o.opi.rot
								s.c.op.
								s.c.rot.
								i.v.op.
								i.v.rot.
								Ketamine
Unit 16								p.o.opi.rot
								s.c.op.
								s.c.rot.
								Ketamine
Unit 17	Yes	Fent + bupi + adr	Low	Tunnelled	Other pall.	Other pall.	Start	s.c.op.
								s.c.rot.
								Ketamine
Unit 18	Yes	Morph + bupi	Close	Tunnelled	Anaest.	Anaest.	Start	p.o.opi.rot
					Nurse pain-team	Nurse pain-team		s.c.op.
								s.c.rot.
								Ketamine
Unit 19	No		Close	Tunnelled	Anaest.	Anaest.	Start	p.o.opi.rot
								s.c.op.
								s.c.rot.
								Ketamine
Unit 20	No		Low	Tunnelled	Anaest.	Anaest.	Start	s.c.op.

Unit 21	Yes	Fent + bupi + adr	Close	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
			Low	Port				s.c.op.
								s.c.rot.
								i.v.op.
Unit 22	No		Close	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
							Await	s.c.op.
								s.c.rot.
Unit 23	No		Close	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
				Port				s.c.op.
								i.v.op.
								Ketamine
Unit 24	Yes	Unknown	Low	Tunnelled	Anaest.	Anaest.	Start	p.o.opi.rot
								s.c.op.
								Ketamine
Unit 25	No		Unknown	Tunnelled	Other pall.	Other pall.	Start	p.o.opi.rot
				Port				s.c.op.
Unit 26	Yes	Fent + bupi + adr	Low	Tunnelled	Other pall.	Other pall.	Await	p.o.opi.rot
								s.c.op.
								Ketamine

PROPOFOL

Question no.:	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**
Unit 1	No	0		No				
Unit 2	No	0		No				
Unit 3	Yes	3	Regular ward	Yes	An.int	An.int	None	None
					An.pall	An.pall	Obs. effect	Obs. effect
						Nurse ward		
Unit 4	Yes	2	Pall. Ward	No	An.int	An.int	RF	None
			ICU			Doctor pall.		
						Nurse pall.		
Unit 5	Yes	6	Regular ward	Yes	An.pall	An.pall	BP/HR	BP/HR
						An.int	SAT	SAT
							RF	RF
Unit 6	Yes	3	Pall. Ward	No	An.int	An.int	RF	RF
					An.pall	An.pall		
						Doctor pall.		
						Nurse pall.		
						Doctor reg.ward		
Unit 7	No	0		No				
Unit 8	Yes	5	Pall. Ward	Yes	An.pall	An.pall	RF	RF
						Nurse pall.	SAT	SAT
Unit 9	No	0		No				
Unit 10	No	0		No				
Unit 11	No	0		No				
Unit 12	No	0		No				
Unit 13	Yes	7	Pall. Ward	No	An.pall	Doctor pall.	RF	None

						Nurse pall.		
Unit 14	Yes	2	Pall. Ward	No	Doctor pall.	Doctor pall.	RF	Other
							SAT	
							Other	
Unit 15	No	0		No				
Unit 16	No	0		No				
Unit 17	No	0		No				
Unit 18	Yes	1	Regular ward	No	An.int	Nurse pall.	BP/HR	SAT
					ICU nurse	Doctor reg.ward	SAT	
							RF	
Unit 19	No	0		No				
Unit 20	No	0						
Unit 21	No	0		Yes				
Unit 22	No	2-3	Regular ward	Yes	An.int	An.int	ECG	
							BP/HR	
							SAT	
							RF	
Unit 23	No	0		No				
Unit 24	Yes	1	ICU	No	An.pall	ICU nurse	ECG	ECG
							BP/HR	BP/HR
							RF	RF
Unit 25	No	0		No				
Unit 26	No	0		No				

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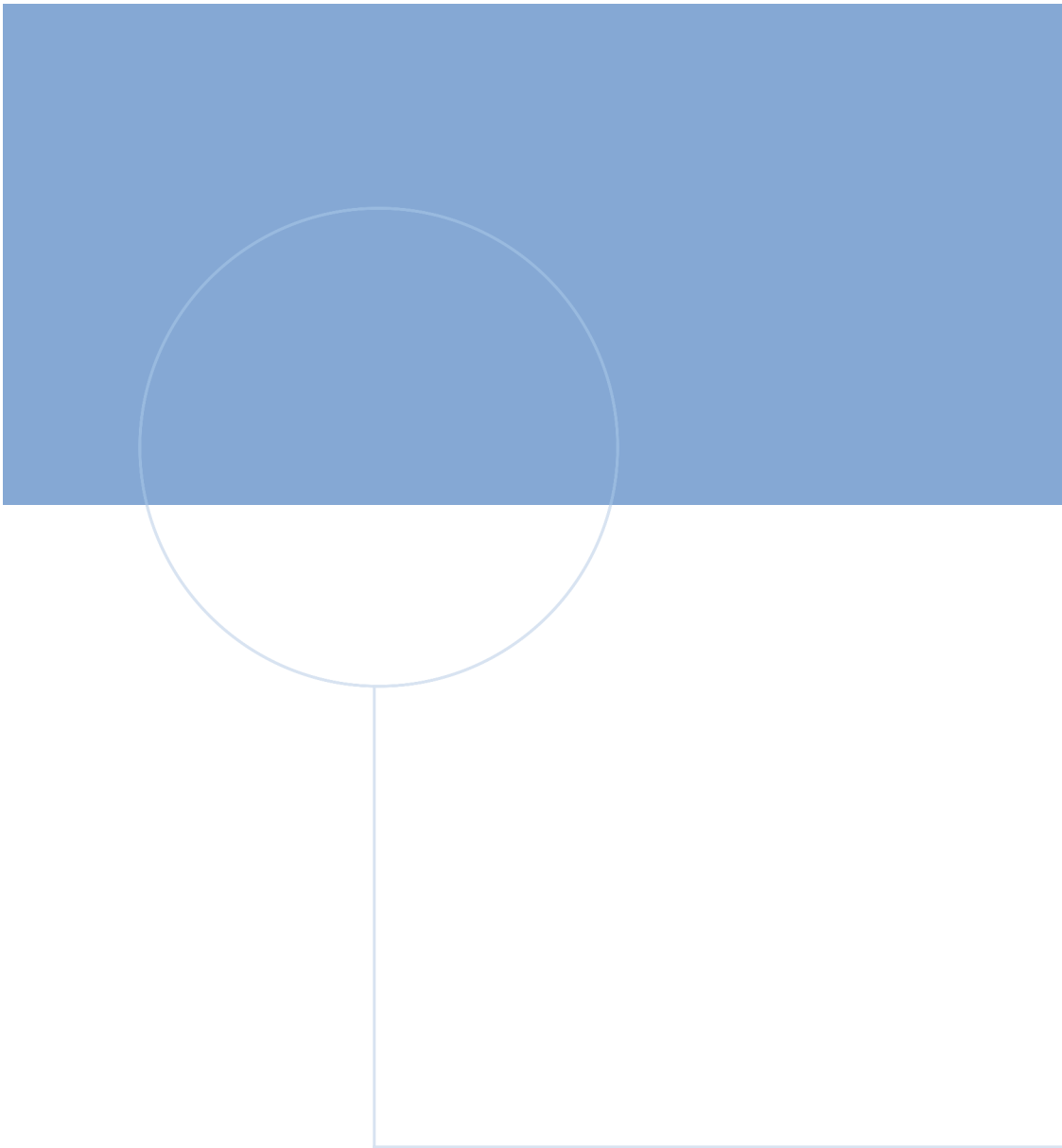

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